Dissertation on

"A STUDY TO DIFFERENTIATE UPPER AND LOWER URINARY TRACT INFECTIONS WITH BLOOD CRP LEVELS"

Submitted in partial fulfillment for the Degree of

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BRANCH – I

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INSTITUE OF INTERNAL MEDICINE
MADRAS MEDICAL COLLEGE
CHENNAI – 600003

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CERTIFICATE

This is to certify that the dissertation titled **"A STUDY TO DIFFERENTIATE UPPER AND LOWER URINARY TRACT INFECTIONS WITH BLOOD CRP LEVELS"** is the bonafide Original work done by **Dr. R.KRISHNA**, post graduate student, Institute of Internal medicine, Madras medical college, Chennai-3, in partial Fulfillment of the University Rules and Regulations for the award of MD Branch -1 General Medicine, under our guidance and supervision, during the academic year 2016 - 2019.

Dr.G.SUNDARAMURTHY M.D.,
Professor of Medicine,
Institute of Internal Medicine
Madras Medical College
RGGGH, Chennai – 600 003,

Prof. Dr.S.TITO M.D.,
Director(i/c) & Professor,
Institute of Internal Medicine
Madras Medical College
RGGGH ,Chennai – 600 003

Prof. Dr. R.JAYANTHI, M.D.,FRCP(GLAS)
DEAN,
Madras Medical College & RGGGH
Chennai 600 003.

DECLARATION

I, **Dr.R.KRISHNA,** solemnly declare that dissertation titled **"A STUDY TO DIFFERENTIATE UPPER AND LOWER URINARY TRACT INFECTIONS WITH BLOOD CRP LEVELS"** is a bonafide work done by me at Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3 during 2017-18 under the guidance and supervision of **Prof. Dr. G.SUNDARAMURTHY, M.D.,** Professor of Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

This dissertation is submitted to Tamilnadu Dr. M.G.R Medical University, towards partial fulfillment of requirement for the award of **M.D.DEGREE IN GENERAL MEDICINE BRANCH-I**.

Place: Chennai -03
Date:

Dr. R.KRISHNA
MD General Medicine,
Post Graduate,
Institute of Internal Medicine,
Madras Medical College,
Chennai – 03

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ABBREVIATION

APN : Acute Pyelonephritis

CBC : Complete Blood Count

CRP : C-Reactive Protein

CT : Computed Tomography

DAMP : Damage Associated Molecular Patterns

DM : Diabetes Mellitus

ESBL : Extended spectrum β lactamase

IDSA : Infectious Diseases Society of America

LTCF : Long Term Care Facilities

MRSA : Methicillin Resistant Staphylococcus Aureus

PAMP :Pathogen Associated Molecular Patterns

SGLT : Sodium-glucose Transporter

SMX : Sulfamethoxazole

TB : Tuberculosis

TMP : Trimethoprim

USG : Ultrasonogram

UTI : Urinary Tract Infection

VUR : Vesico-Ureteric Reflux

WBC : White Blood Cells

XGP : Xanthogranulomatous Pyelonephritis

CONTENTS

INTRODUCTION

Urinary tract infection may involve only the lower urinary tract or both the upper and lower tracts. The term *cystitis* has been used to describe the syndrome involving dysuria, frequency, urgency, and occasionally suprapubic tenderness. However, these symptoms may be related to lower tract inflammation without bacterial infection and can be caused by urethritis (e.g., gonorrhea or chlamydial urethritis). Furthermore, the presence of symptoms of lower tract infection without upper tract symptoms by no means excludes upper tract infection, which is also often present. Acute pyelonephritis describes the clinical syndrome characterized by flank pain, tenderness, or both, and fever, often associated with dysuria, urgency, and frequency. However, these symptoms can occur in the absence of infection (e.g., in renal infarction or renal calculus).A more rigorous definition of acute pyelonephritis is the previously described syndrome accompanied by significant bacteriuria and acute infection in the kidney. Uncomplicated urinary tract infection refers to infection in a structurally and neurologically normal urinary tract. Complicated urinary tract infection refers to infection in a urinary tract with functional or structural abnormalities, including indwelling catheters and calculi[1]. In general, infection in men, pregnant women, children, and patients who are hospitalized or in health care–

associated settings may be considered complicated. In the patient with complicated infection, infecting microorganisms are more likely to be resistant to antimicrobial agents.

AIMS AND OBJECTIVES

To explore a diagnostic method to differentiate for upper and lower urinary tract Infections.

REVIEW OF LITERATURE

Urinary tract infection

In adults UTI can be classified into 5 groups[2]

- Uncomplicated cystitis in women
- Recurrent cystitis in women
- Acute uncomplicated pyelonephritis in women
- Complicated UTI
- Asymptomatic bacteriuria

Complicated UTI

It is defined as urinary tract infection that increases risk for serious complications or treatment failure.

Complicated UTIs may require different pre treatment and post treatment evaluation and duration of anti-microbial treatment than for UN complicated UTI. Occasionally complicated UTIs are diagnosed after a poor response to treatment.

Factors modulating risk of acute uncomplicated urinary tract infections in women:

Host Determinants	Uropathogen Determinants
Behavioral: Sexual intercourse, use of spermicidal products, recent antimicrobial use, suboptimal voiding habits	*Escherichia coli* virulence determinants: P, S, Dr, and type 1 fimbriae; hemolysin; aerobactin; serum resistance
Genetic: Innate and adaptive immune response, enhanced epithelial cell adherence, antibacterial factors in urine and bladder mucosa, nonsecretor of ABO blood group antigens, P1 blood group phenotype, reduced *CXCR1* expression, previous history of recurrent cystitis	
Biologic: Estrogen deficiency in postmenopausal women, glycosuria (including from SGLT-1 inhibitors)	

picture 1:Factors complicating Uncomplicated UTI in women

Epidemiology

The incidence of acute cystitis in sexually active women is about 0.5 per 1 person year[3]. The incidence of acute pyelonephritis in young women is about 3/1000 person –years[4]. The incidence of symptomatic urinary tract infection in adult men less than 50 years is much lower than seen in women ranging from 5 to 8 /10000 men annually.

Nosocomial urinary tract infections are a common cause of complicated UTI which occurs in 5% of admission in tertiary care hospitals. In hospitalized patients , catheter associated bacteriuria is the most common source of gram-negative bacteremia[5].

Asymptomatic bacteriuria is defined as presence of 10^5 or more colony forming units per ml of the organism in 2 separate consecutive clean voided urine specimen in the absence of symptom related to the urinary tract[6]. It is found in about 5% of adult young women[7] and very rarely in men less than 50 years.

Pathogenesis

Uncomplicated infection

Most of uncomplicated UTIs in healthy women result when organisms such as E.coli present in rectum enter the urinary bladder after an interim phase of distal urethral colonization. Staphylococcus aureus seed the urinary tract by hematogeneous spread.

The protective factors from urinary tract infection include

- Host‘s immune response
- Maintanence of normal vaginal flora
- Removal of urinary bladder bacteriuria by micturition[8] .

P-fimbriated Strains of Escherichia coli are associated with acute uncomplicated pyelonephritis. Their adherence properties stimulate epithelial and other cells to produce inflammatory factors that stimulate the inflammatory response[9] .

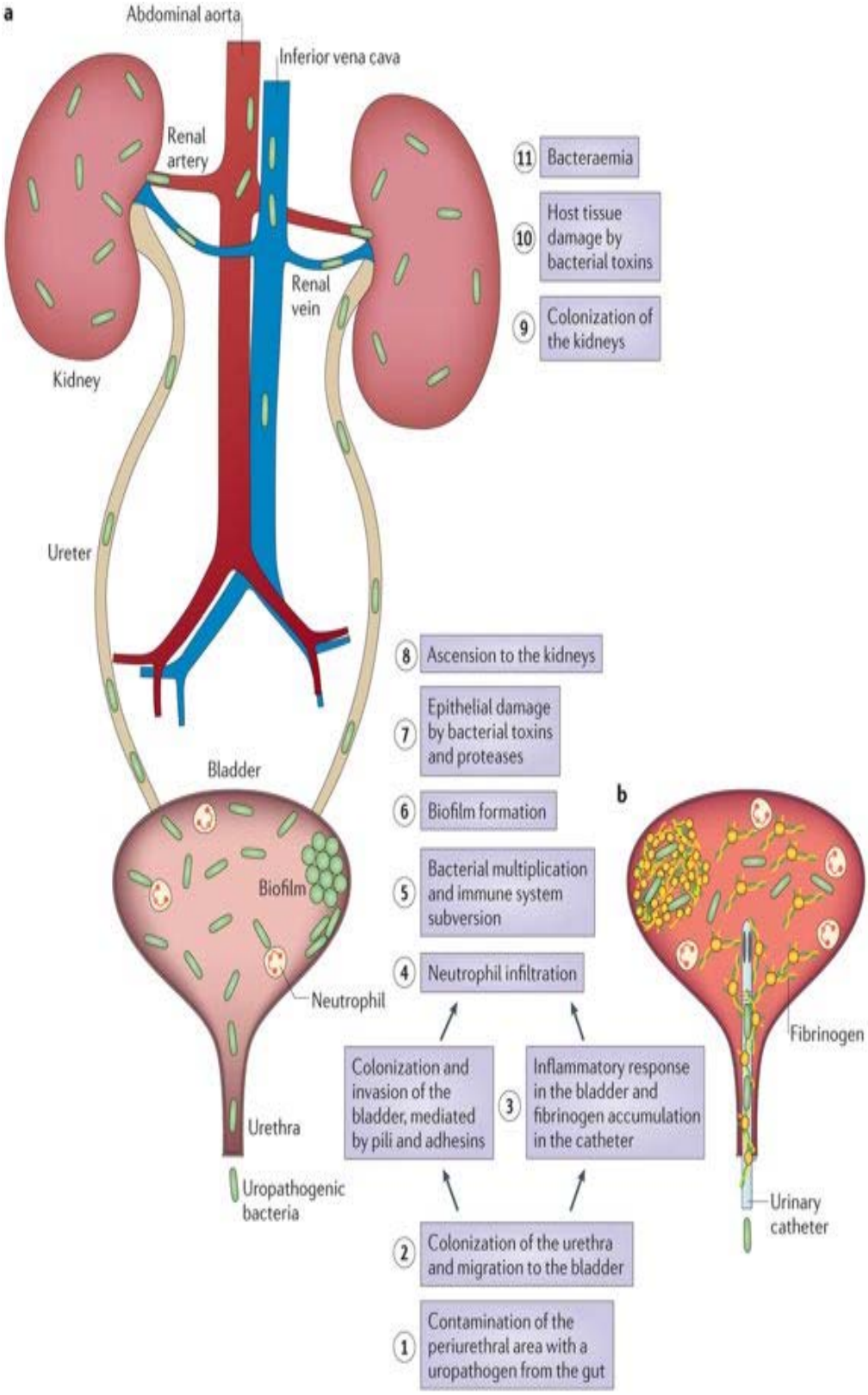

a
Abdominal aorta
Inferior vena cava
Renal artery
Renal vein
Kidney
Ureter
Bladder
Biofilm
Neutrophil
Urethra
Uropathogenic bacteria
11 Bacteraemia
10 Host tissue damage by bacterial toxins
9 Colonization of the kidneys
8 Ascension to the kidneys
7 Epithelial damage by bacterial toxins and proteases
6 Biofilm formation
5 Bacterial multiplication and immune system subversion
4 Neutrophil infiltration
3 Inflammatory response in the bladder and fibrinogen accumulation in the catheter
Colonization and invasion of the bladder, mediated by pili and adhesins
2 Colonization of the urethra and migration to the bladder
1 Contamination of the periurethral area with a uropathogen from the gut
b
Fibrinogen
Urinary catheter

Figure 2.

The determinants of virulence include

- Adherence factor (type 1, S, and Dr fimbriae)
- Toxins(hemolysin)
- Immune evasion
- Iron acquisition(aerobactin)
- Flagella
- serum resistance [10]

The factors responsible for decreased prevalence of UTI in men include;

i. Greater distance between the anus and the urethral meatus
ii. Drier environment surrounding male urethra
iii. Greater length of male urethra

Risk factors for urinary tractinfection in young healthy men include;

- Intercourse with an infected female partner
- Anal intercourse
- Lack of circumcision

Complicated infection ;

The predisposing factors that lead to complicated UTI include;

- Obstruction or stasis of urine flow
- Facilatiting entry of organisms into urinary tract by bypassing host defence mechanisms
- Providing a nidus for infection not readily treatable with antimicrobials
- Compromising the host immune system

Complicated UTIs occur in settings of impaired host defence such as

- Indwelling catheter use
- VUR
- Obstruction
- Neutropenia
- Immune deficiencies

Diabetes mellitus is associated with syndromes of complicated UTI including

1. Renal and perirenal abscess
2. Emphysematous pyelonephritis and cystitis
3. Papillary necrosis
4. Xanthogranulomatous pyelonephritis

The virulence of the pathogens are less important in the pathogenesis of complicated urinary tract infections compared with uncomplicated urinary tract infections.But,multidrug resistance is more likely with complicated urinary tract infections.

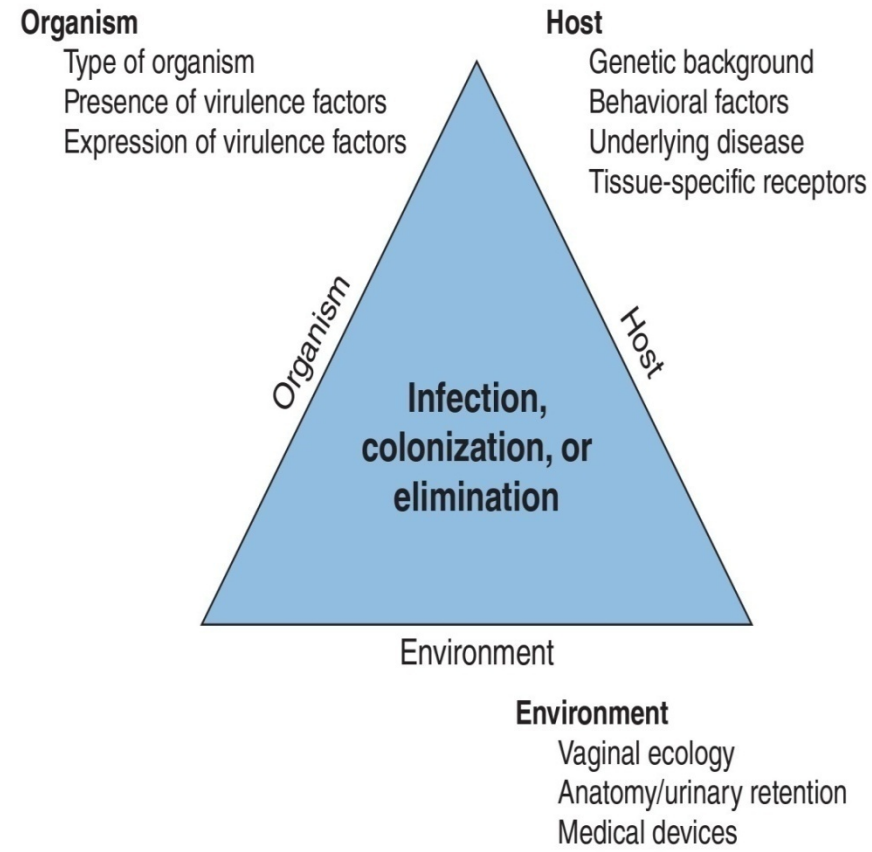


FIGURE 162-1 Pathogenesis of urinary tract infection. The relationship among specific host, pathogen, and environmental factors determines the clinical outcome.

Figure 3.

ETIOLOGICAL AGENTS;

BACTERIAL ETIOLOGY OF URINARY TRACT INFECTIONS

Organisms	URINARY TRACT INFECTION (%) Uncomplicated	Complicated
Gram-Negative Organisms		
Escherichia coli	70-95	21-54
Proteus mirabilis	1-2	1-10
Klebsiella spp.	1-2	2-17
Citrobacter spp.	<1	5
Enterobacter spp.	<1	2-10
Pseudomonas aeruginosa	<1	2-19
Other	<1	6-20
Gram-Positive Organisms		
Coagulase-negative staphylococci (*Staphylococcus saprophyticus*)	5-20 or more	1-4
Enterococci	1-2	1-23
Group B streptococci	<1	1-4
Staphylococcus aureus	<1	1-2
Other	<1	2

Picture 4:Bacterial organisms causing UTI

Uncomplicated upper and lower urinary tract infections are most often caused by Escherichia coli in 70% to 95% and staphylococcus saphrophyticus present in 5% to 20%. The common contaminants in healthy non-pregnant women include lactobacilli, enterococci, coagulase negative staphylococcus and group B streptococci.

E.coli is the most common bacteria in complicated UTIs. Other organisms include citrobacter spp.,Enterobacter spp., enterococci, pseudomonas aeruginosa,staph.aureus. UTIs caused by fungi ,especially candida spp., is increasing. Polymicrobial and multidrug resistant infections are more likely in patients with chronic conditions such as neurogenic bladder and spinal cord injury.

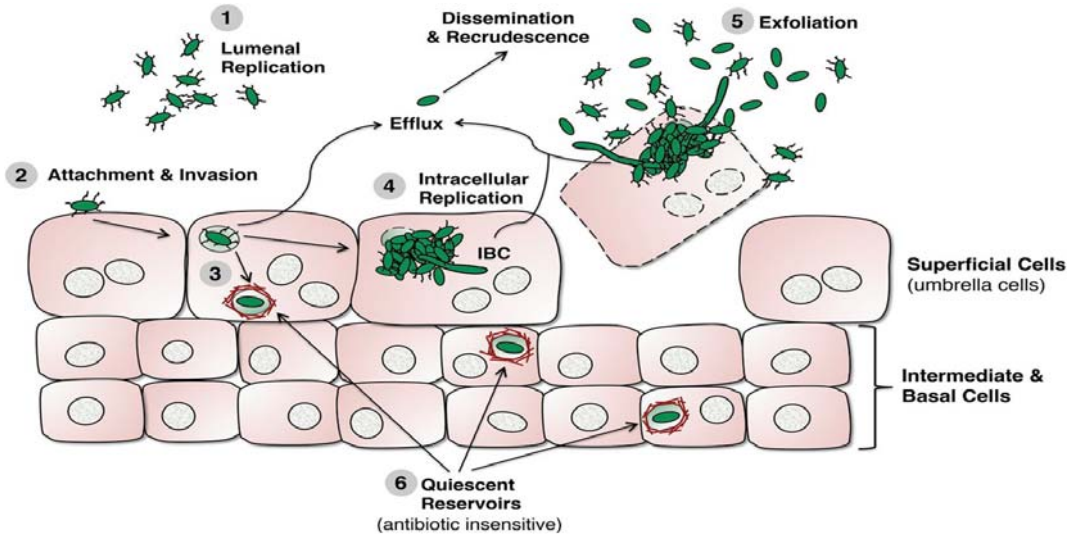


Figure 5. Factors that promote the recurrence of UTI

CLINICAL SYNDROMES

- Acute uncomplicated cystitis in healthy women
- Recurrent acute uncomplicated cystitis in healthy women
- Acute uncomplicated pyelonephritis in healthy women
- Complicated urinary tract infection*
  - Male sex
  - Pregnancy
  - Poorly controlled diabetes mellitus
  - Obstruction or other structural factor: Urolithiasis, malignancies, ureteral and urethral strictures, bladder diverticula, renal cysts, fistulas, ileal conduits, other urinary diversions
  - Functional abnormality: Neurogenic bladder, vesicoureteral reflux
  - Foreign bodies: Indwelling catheter, ureteral stent, nephrostomy tube
  - Other conditions: Renal failure, renal transplantation, immunosuppression, multidrug-resistant uropathogens, health care–associated (includes hospital-acquired/LTCF-acquired) infection, prostatitis-related infection, upper tract infection in an adult other than a healthy woman, other functional or anatomic abnormality of urinary tract)
- Asymptomatic bacteriuria

Figure 6.

Acute uncomplicated cystitis in young women;

They present with symptoms such as acute onset of dysuria,frequency,urgency or suprapubic pain. In a sexually active young women acute cystitis usually presents with acute dysuria. Neisseria gonorrhoeae,chlamydia trachomatis,or herpes simplex virus infections presents with acute urethritis. Candida spp. Or Trichomonas vaginalis presents with vaginitis.Definitive diagnosis of urinary tract infection

requires the presence of significant bacteriuria ,which is 10^5 or more uropathogens per ml of midstream voided urine. The IDSA (Infectious Diseases Society of America) consensus definition of cystitis is 10^3 cfu per milliliter or more uropathogens[11].Generally,urine cultures are not required in women with uncomplicated cystitis because patient's history is highly reliable in establishing the diagnosis[12].

Increasing resistance is often encountered for E.coli in uncomplicated UTIs to sulfonamides, amoxicillin, cotrimoxazole. Nitrofurantoin resistance to E.coli is less than 5%,although it is inactive against proteus spp. And some klebsiella spp and Enterobacter.In uncomplicated cystitis, E.coli strains are susceptible to fluoroquinolones although resistance is increasing in many parts of the world[13,14]. Infections caused by ESBL (extended spectrum β-lactamase) producing strains are increasing in number in addition,even in the setting of uncomplicated urinary tract infection.

Recurrent Acute Uncomplicated Cystitis in Women

Much recurrent cystitis in healthy women is caused by persistence of the initially infecting strain in the fecal flora[15]. Experimental studies in mice also suggest that some same-strain recurrent UTIs may be caused by a latent reservoir of uropathogens in the bladder

epithelium that persist after the initial UTI[16], and indirect evidence indicates that this may occur in humans[17]. If the recurrence is within 1 or 2 weeks of treatment, an antimicrobial-resistant uropathogen should be considered, and a urine culture should be performed followed by treatment with an alternative regimen.

Acute Uncomplicated Pyelonephritis in Women

Acute pyelonephritis is suggested by fever (temperature ≥38° C), chills, flank pain, nausea and vomiting, and costovertebral angle tenderness. Cystitis symptoms are variably present. Symptoms may vary from a mild illness to a sepsis syndrome with or without shock and renal failure. Pyuria is almost always present, but leukocyte casts, specific for UTI, are infrequently seen. Gram stain of the urine sediment may aid in differentiating gram-positive and gram-negative infections, which can influence empiric therapy. A urine culture, which should be performed in all women with acute pyelonephritis, will have 10^4 cfu/ml or more of uropathogens in up to 95% of patients[11]. On pathologic examination, the kidney shows a focal inflammatory reaction with neutrophil and monocyte infiltrates, tubular damage, and interstitial edema . Although imaging studies are generally not performed, the infected kidney is often enlarged, and contrast enhanced computed tomography (CT) shows

decreased opacification of the affected parenchyma, typically in patchy, wedge-shaped, or linear patterns.

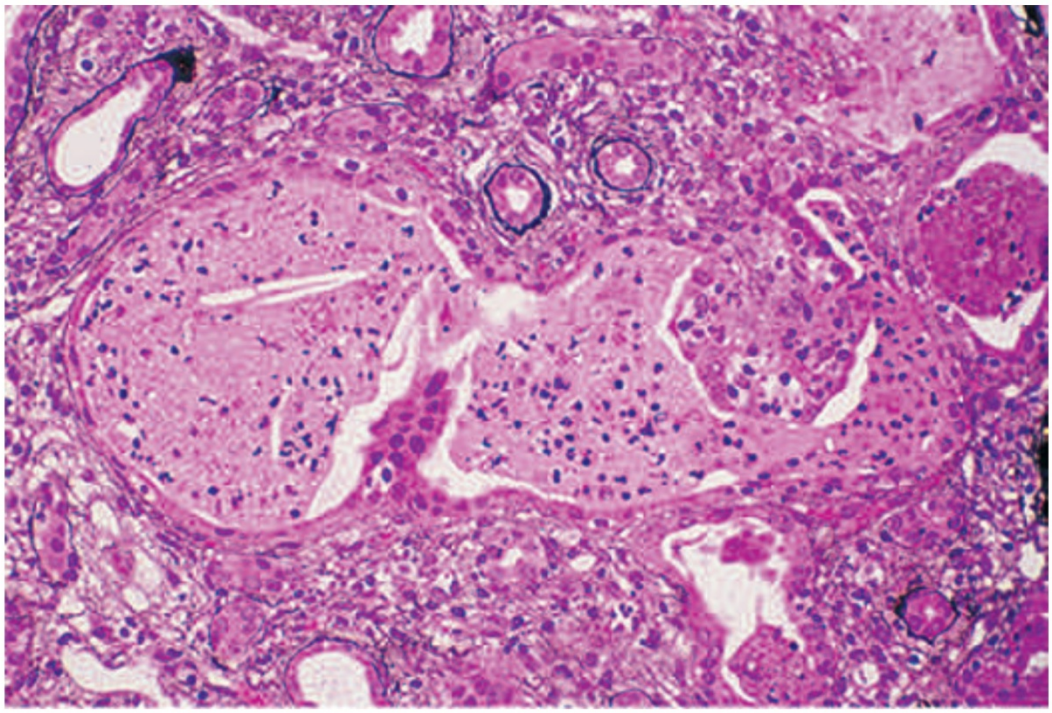


Fig. 51.3 Acute pyelonephritis. Renal tissue shows a dilated tubule with neutrophils enmeshed in proteinaceous debris ("pus casts") with adjacent interstitial inflammation. (Courtesy C. Alpers, University of Washington, Seattle, Wash.)

Picture 6:Histopathology of Acute Pyelonephritis

Complicated Infections

Patients with complicated UTI may present with classic signs of cystitis and pyelonephritis but also may have vague or nonspecific symptoms, such as fatigue, irritability, nausea, headache, and abdominal or back pain. Acute cystitis in healthy individuals other than young women is more likely to involve occult renal or prostatic infection and may respond poorly to short-course therapy. Noninvasive tools to localize

infections to the kidney or prostate are lacking, so clinical estimation of risk in a given patient is imprecise. Some patients, such as those who are diabetic or pregnant, warrant special attention because of the serious complications that can occur if treatment is inadequate. Urethritis must be excluded in dysuric sexually active men by a urethral Gram stain or a first-voided urine specimen wet-mount evaluation for urethral leukocytosis.

Complicated UTI, as with uncomplicated infection, is generally associated with pyuria and bacteriuria, although these may be absent if the infection does not communicate with the collecting system.

Urine culture should always be performed in patients with suspected complicated UTI. The IDSA consensus definition of complicated UTI is 10^5 cfu/ml or more in the urine of women and 10^4 cfu/ml or more in men, but lower counts in symptomatic persons, as demonstrated in patients with uncomplicated UTI, may well represent significant bacteriuria. This is especially true when the specimen is collected from a urinary catheter. Thus it is reasonable to use a colony count threshold of 10^3 cfu/ml of uropathogens to diagnose complicated UTI.

Catheter-Associated Infections;

Approximately 15% to 25% of patients in general hospitals have a urethral catheter inserted at some time during their stay, and approximately 5% to 10% of long-term care facility residents are managed with urethral catheterization, in some cases for years. The incidence of bacteriuria associated with indwelling catheters is 3% to 10% per day of catheterization, and the duration of catheterization is the most important risk factor for the development of catheter-associated bacteriuria.

Catheter-associated bacteriuria is the most common source of gram negative bacteremia in hospitalized patients. Complications of long-term catheterization (≥30 days) include almost universal bacteriuria, often with multiple antibiotic-resistant flora, and (in addition to cystitis, pyelonephritis, and bacteremia, as seen with short-term catheterization) frequent febrile episodes, catheter obstruction, stone formation associated with urease-producing uropathogens, and local genitourinary infections. Other rare complications include fistula formation and bladder cancer. An increase in mortality risk has been reported with catheter associated bacteriuria, but it is difficult to distinguish the role of the catheter because most deaths occur in patients who have severe underlying disease.

Spinal Cord Injury;

Spinal cord injury alters the dynamics of voiding and often requires the use of bladder drainage with catheters. The diagnosis of UTI in patients with spinal cord injuries is often problematic and is based on the combination of symptoms and signs (which are often nonspecific), pyuria, and significant bacteriuria.

Prostatitis;

Prostatitis occurs in up to 25% of men during their lifetime, but it is caused by acute or chronic bacterial infection in a minority[18].

The most common organisms causing bacterial prostatitis are gram-negative bacilli, including *E. coli*, *Proteus* spp., *Klebsiella* spp., *P.aeruginosa*, and, less frequently, enterococci and *S. aureus*. The pathogenesis of prostatitis is believed to be related to reflux of infected urine from the urethra into the prostatic ducts. Prostatic calculi, commonly found in adult men, may provide a nidus for bacteria and protection from antibacterial agents.Acute bacterial prostatitis is rare. Patients present with dysuria, frequency,urgency, obstructive voiding symptoms, fever, chills, and myalgias.The prostate is tender and swollen. Prostatic massage, as a diagnostic test, is contraindicated in men in whom the diagnosis of acute prostatitis is being considered because of the risk

for precipitating bacteremia. The patient will usually have pyuria and a positive urine culture.re usually present in quantities of 10^5 cfu/ml or more.

Chronic bacterial prostatitis is characterized by recurrent UTIs with the same uropathogen with intervening asymptomatic periods. The prostate typically is normal to palpation during asymptomatic periods.Chronic bacterial prostatitis is characterized microscopically by the presence of 10 or more leukocytes per high-power field in expressed prostatic secretions or postmassage voided urine in the absence of significant pyuria in first-voided and midstream urine specimens, as well as a uropathogen colony count at least 10-fold higher in the expressed prostatic secretions or postmassage voided urine compared with the first-voided midstream urine. In addition, macrophage-laden fat droplets (oval fat bodies) are usually prominent in the prostatic secretions.

Renal Abscess;

Renal cortical and cortico medullary abscesses and perirenal abscesses occur in 1 to 10 per 10,000 hospital admissions[19] .Patients usually present with fever, chills, back or abdominal pain, and costovertebral angle tenderness, but they may have no urinary symptoms or findings if the abscess does not communicate with the collecting system, as often occurs with a cortical abscess. Bacteremia may be

primary (cortical abscess) or secondary (corticomedullary or perirenal). The clinical presentation may be insidious and nonspecific, especially with perirenal abscess, and the diagnosis may not be made until admission to a hospital or at autopsy. CT is recommended to establish the diagnosis and location of a renal or perirenal abscess. A *renal cortical abscess* (renal carbuncle) is usually caused by *S.aureus,* which reaches the kidney by hematogenous spread. A *renal corticomedullary abscess,* in contrast, usually results from ascending UTI in association with an underlying urinary tract abnormality, such as obstructive uropathy or VUR, and is usually caused by common uropathogenic species such as *E. coli* and other gram-negative bacilli. Such abscesses may extend deep into the renal parenchyma, perforate the renal capsule, and form a perirenal abscess. Perirenal abscesses usually occur in the setting of obstruction or other complicating factors and result from ruptured intrarenal abscesses, hematogenous spread, or spread from a contiguous infection. Causative uropathogens are those usually found in complicated UTIs, including *S. aureus* and enterococci; polymicrobial infections are common. Anaerobes or *Mycobacterium tuberculosis* may be causative.

Papillary Necrosis

More than half of patients who develop papillary necrosis have diabetes, almost always in conjunction with a UTI, but the condition also complicates sickle cell disease, analgesic abuse, and obstruction. Renal papillae are vulnerable to ischemia because of the sluggish blood flow in the vasa recta, and relatively modest ischemic insults may cause papillary necrosis. The clinical features are those typical of pyelonephritis. In addition, passage of sloughed papillae into the ureter may cause renal colic, renal impairment or failure, or obstruction with severe urosepsis. Papillary necrosis in the setting of pyelonephritis is associated with pyuria and a positive urine culture. Causative uropathogens are those typical of complicated UTI. CT is the preferred diagnostic procedure. Radiologic findings include an irregular papillary tip; dilated calyceal fornix; extension of contrast material into the parenchyma; and a separated crescent-shaped papilla surrounded by contrast, called the *ring sign*

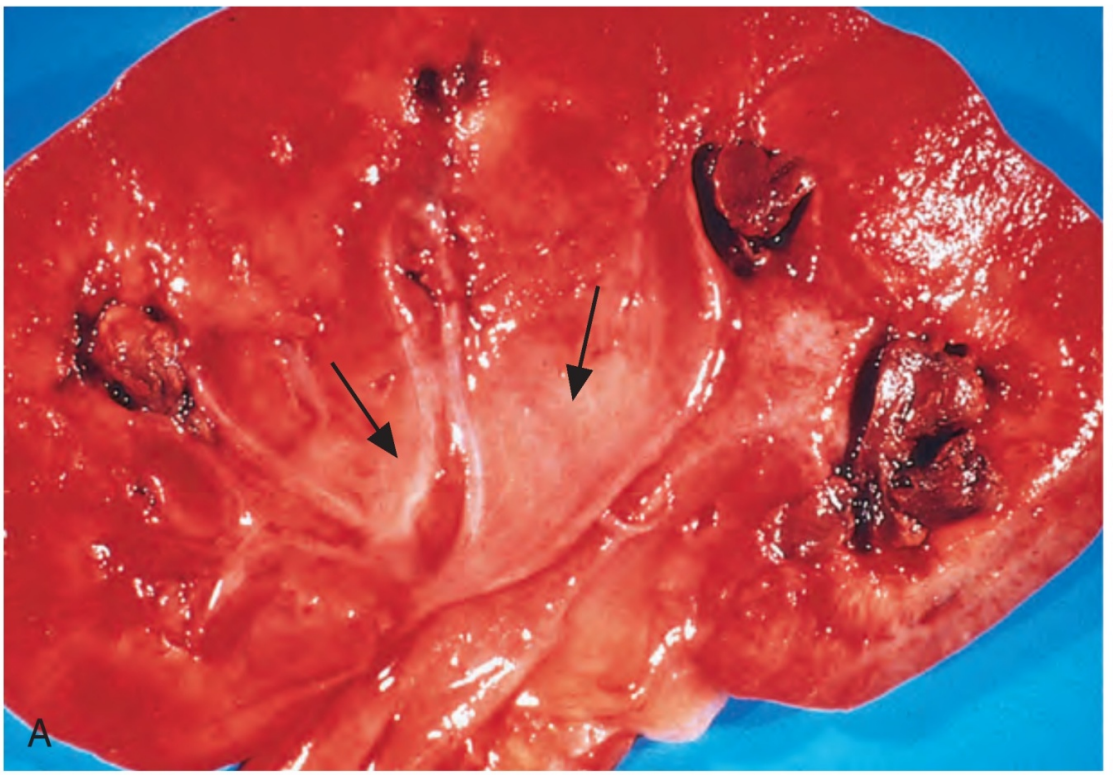


Figure 20-29 Papillary necrosis. Areas of pale-gray necrosis involve the papillae *(arrows)*.

Figure 7.

Emphysematous Pyelonephritis

Emphysematous pyelonephritis is a fulminant, necrotizing, life-threatening variant of acute pyelonephritis caused by gas-forming organisms, including *E. coli, Klebsiella pneumoniae, P. aeruginosa,* and *Proteus mirabilis*[20]. Up to 90% of cases occur indiabetic patients, and obstruction may be present. Symptoms are suggestive of pyelonephritis, and there may be a flank mass. Dehydration and ketoacidosis are common. Pyuria and a positive urine culture are usually present. Gas is usually detected by a plain abdominal radiograph or ultrasound . CT is

the diagnostic modality of choice, however, because it can localize the gas better than ultrasound. Accurate localization of gas is important because gas also may form in an infected obstructed collecting system or renal abscess; although serious, these conditions do not carry the same poor prognosis and are managed differently.

Renal Malacoplakia

Malacoplakia is a chronic granulomatous disorder of unknown etiology involving the genitourinary, gastrointestinal, skin, and pulmonary systems[21]. It is characterized by an unusual inflammatory reaction to a variety of infections and is manifested by the accumulation of macrophages containing calcified bacterial debris called *Michaelis-Gutmann bodies* . The underlying disorder appears to be a monocyte-macrophage bactericidal defect. The diagnosis is made by histologic examination of involved tissue. Genitourinary malacoplakia, most often involving the bladder, is usually associated with gram-negative UTI. Patients with renal malacoplakia generally have fever, flank pain, pyuria and hematuria, bacteriuria, and, if both kidneys are involved, impaired renal function. CT usually shows enlarged kidneys with areas of poor enhancement, and the condition may be indistinguishable from other infectious or neoplastic lesions. On occasion, the malacoplakia may

extend through the renal capsule into the perinephric space, simulating a renal carcinoma.

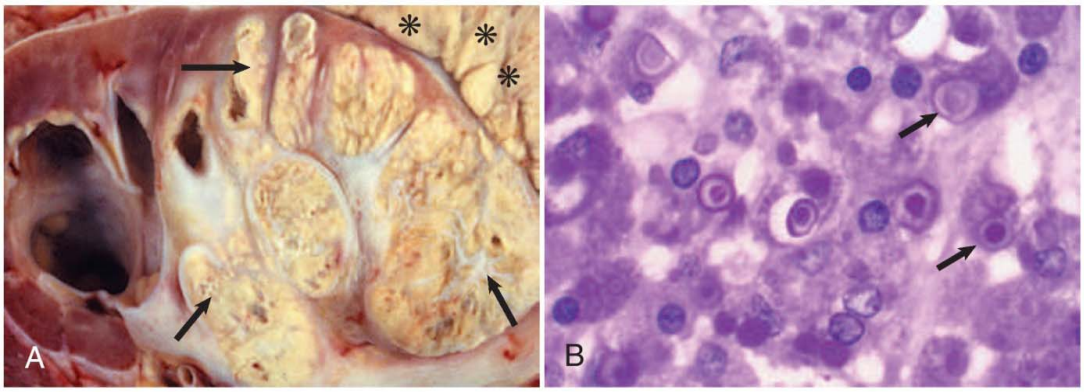


Fig. 51.8 Renal malacoplakia. (A) Malacoplakia involving most of the kidney *(arrows)* with extension through the capsule *(asterisks)*. A small portion of normal kidney is present associated with hydronephrosis secondary to obstruction by the malacoplakia. (B) The kidney tissue shows many macrophages containing intracytoplasmic inclusions (*arrows* identify two particularly well-demarcated macrophages with Michaelis-Gutmann bodies). (Courtesy L. Truong, Baylor College of Medicine, Houston, Tex, and N. Sheerin, Guy's Hospital, London.)

Picture 8:Renal Malacoplakia

Xanthogranulomatous Pyelonephritis

Xanthogranulomatous pyelonephritis is a poorly understood, uncommon but severe chronic destructive granulomatous inflammation of renal parenchyma associated with obstruction and infection of the urinary tract[22]. The renal parenchyma is replaced with a diffuse or segmental cellular infiltrate of foam cells, which are lipid-laden macrophages. The process also may extend beyond the renal capsule to the retroperitoneum. Its pathogenesis appears to be multifactorial, with infection complicating obstruction and leading to ischemia, tissue destruction, and accumulation of lipid deposits. Patients with xanthogranulomatous pyelonephritis are characteristically middle-aged women and have chronic symptoms such

as flank pain, fever, chills, and malaise. Flank tenderness, a palpable mass, and irritative voiding symptoms are common. The urine culture is usually positive with *E. coli,* other gram-negative bacilli, or *S. aureus*. CT generally shows an enlarged nonfunctioning kidney, often the presence of calculi and low-density masses (xanthomatous tissue), and in some cases, involvement of adjacent structures . It may be difficult to distinguish from neoplastic disease.

Asymptomatic Bacteriuria

Asymptomatic bacteriuria is common and generally benign. Pyuria is often present, especially in elderly people, and is a predictor for subsequent symptomatic UTI in some groups. Causative uropathogens are the same as those causing UTIs in the same population. Screening for and treatment of asymptomatic bacteriuria is generally not warranted. In young women with recurrent UTI, asymptomatic bacteriuria may be protective against symptomatic recurrence and treatment may increase the risk for such recurrences[23]. However, patients at high risk for serious complications warrant a more aggressive approach to diagnosis and treatment, including pregnant women and patients undergoing urologic surgery. Current management strategies in patients with a renal transplant, including long-term antimicrobial prophylaxis, help prevent both asymptomatic bacteriuria and symptomatic UTI. It is not clear,

however, whether screening for or treatment of asymptomatic bacteriuria in such patients is worthwhile. Some authorities advise treatment of asymptomatic bacteriuria found in patients with anatomic or functional abnormalities of the urinary tract, diabetic patients, and patients with urea-splitting bacteria (e.g., *P. mirabilis, Klebsiella* spp.). Evidence based guidelines for screening and treatment of asymptomatic bacteriuria in these populations are needed.Asymptomatic bacteriuria in catheterized patients in hospitals and longterm care facilities, although thought to be generally benign, represents a large reservoir of antimicrobial-resistant urinary pathogens that increases the risk for cross-infection among catheterized patients and results in frequent inappropriate antimicrobial use[24].

INVESTIGATIONS;

Urinalysis

specimen collection

Specimens must be collected in clean, dry, leak-proof containers.

Disposable containers should be used because they eliminate the chance of contamination owing to improper washing. These disposable containers are available in a variety of sizes and shapes, including bags with adhesive for the collection of pediatric specimens and large

containers for 24-hour specimens. Properly applied screw-top lids are less likely to leak than are snap-on lids. Containers for routine urinalysis should have a wide mouth to facilitate collections from female patients and a wide,flat bottom to prevent overturning. They should be made of a clear material to allow for determination of color and clarity. The recommended capacity of the container is 50 mL, which allows 12 mL of specimen needed for microscopic analysis, additional specimen for repeat analysis, and enough room for the specimen to be mixed by swirling the container. Individually packaged sterile containers with secure closures should be used for microbiologic urine studies. Sterile containers are also suggested if more than 2 hours elapse between specimen collection and analysis. Specially designed sterile containers are available that have a lid with a transfer device that can be assessed with a device called a transfer straw. The transfer straw has a needle and an evacuated tube holder. Urine can be sterilely transferred to tubes containing preservatives for microbiology testing and tubes with conical bottoms for sediment analysis or round bottoms for automated reagent strip testing.

Specimen Preservation

The most routinely used method of preservation is refrigeration at 2°C to 8°C, which decreases bacterial growth and metabolism. If the urine is to be cultured, it should be refrigerated during transit and kept

refrigerated until cultured up to 24 hours. The specimen must return to room temperature before chemical testing by reagent strips. When a specimen must be transported over a long distance and refrigeration is impossible, chemical preservatives may be added. Commercially prepared transport tubes are available. The ideal preservative should be bactericidal, inhibit urease, and preserve formed elements in the sediment. The most routinely used method of preservation is refrigeration at 2°C to 8°C, which decreases bacterial growth and metabolism. If the urine is to be cultured, it should be refrigerated during transit and kept refrigerated until cultured up to 24 hours. The specimen must return to room temperature before chemical testing by reagent strips. When a specimen must be transported over a long distance and refrigeration is impossible, chemical preservatives may be added. Commercially prepared transport tubes are available. The ideal preservative should be bactericidal, inhibit urease, and preserve formed elements in the sediment.

Midstream Clean-Catch Specimen

As an alternative to the catheterized specimen, the midstream clean-catch specimen provides a safer, less traumatic method for obtaining urine for bacterial culture and routine urinalysis. It provides a specimen that is less contaminated by epithelial cells and bacteria and,

therefore, is more representative of the actual urine than the routinely voided specimen. Patients must be provided with appropriate cleansing materials, a sterile container, and instructions for cleansing and voiding. Strong bacterial agents, such as hexachlorophene or povidone-iodine, should not be used as cleansing agents. Mild antiseptic towelettes are recommended. Some urine collection transfer kits contain Castile Soap Towelettes.

Suprapubic Aspiration

Occasionally urine may be collected by external introduction of a needle through the abdomen into the bladder. Because the bladder is sterile under normal conditions, suprapubic aspiration provides a sample for bacterial culture that is completely free of extraneous contamination. The specimen can also be used for cytologic examination.

Bacteria

Bacteria are not normally present in urine. However, unless specimens are collected under sterile conditions (catheterization), a few bacteria are usually present as a result of vaginal, urethral, external genitalia, or collection-container contamination. These contaminant bacteria multiply rapidly in specimens that remain at room temperature for extended periods, but are of no clinical significance. They may

produce a positive nitrite test result and also frequently result in a pH above 8, indicating an unacceptable specimen. Bacteria may be present in the form of cocci (spherical) or bacilli (rods). Owing to their small size, they must be observed and reported using high-power magnification. They are reported as few, moderate, or many per high-power field.To be considered significant for UTI, bacteria should be accompanied by WBCs. Some laboratories report bacteria only when observed in fresh specimens in conjunction with WBCs . The presence of motile organisms in a drop of fresh urine collected under sterile conditions correlates well with a positive urine culture. Observing bacteria for motility also is useful in differentiating them from similarly appearing amorphous phosphates and urates. The use of phase microscopy aids in the visualization of bacteria.

Microscopic Examination

Much can be learned from simple microscopic examination of urine. A drop of fresh uncentrifuged urine placed on a slide, covered with a coverglass, and examined with restricted light intensity under the high-dry objective of an ordinary clinical microscope can reveal leukocytes, epithelial cells, and bacteria if more than 10^5/mL are present. Finding 10^5 organisms per milliliter in a properly collected and examined urine specimen is strong evidence of active urinary tract infection. A Gram

stained smear of uncentrifuged midstream urine that shows gram-negative rods is diagnostic of a urinary tract infection.

Brief centrifugation of urine readily sediments pus cells, which may carry along bacteria and thus may help in microscopic diagnosis of infection. The presence of other formed elements in the sediments—or the presence of proteinuria—is of little direct aid in the specific identification of active urinary tract infection. Pus cells may be present without bacteria, and, conversely, bacteriuria may be present without pyuria. The presence of many squamous epithelial cells, lactobacilli, or mixed flora on culture suggests improper urine collection. Some urine dipsticks contain leukocyte esterase and nitrite, measurements of polymorphonuclear cells and bacteria, respectively, in the urine. Positive reactions are strongly suggestive of bacterial urinary tract infection. Although not readily embraced by clinical microbiology laboratories, many chemistry laboratories have implemented automated or semiautomated instruments for routine performance of urinalysis. A variety of techniques are used by these instruments to detect leukocytes and bacteria. The performance of these systems varies, but they bring a level of standardization for high-volume testing that may not be accomplished using dipstick methods.

Culture

Culture of the urine, to be meaningful, must be performed quantitatively. Properly collected urine is cultured in measured amounts on solid media, and the colonies that appear after incubation are counted to indicate the number of bacteria per milliliter. The usual procedure is to spread 0.001–0.05 mL of undiluted urine on blood agar plates and other solid media for quantitative culture. All media are incubated overnight at 37°C; growth density is then compared with photographs of different densities of growth for similar bacteria, yielding semiquantitative data. In active pyelonephritis, the number of bacteria in urine collected by ureteral catheter is relatively low. While accumulating in the bladder, bacteria multiply rapidly and soon reach numbers in excess of 105/mL—far more than could occur as a result of contamination by urethral or skin microbiota or from the air. Therefore, it is generally agreed that if more than 10^5 colonies/mL are cultivated from a properly collected and properly cultured urine specimen, this constitutes strong evidence of active urinary tract infection. The presence 10^5 bacteria or more of the same type per milliliter in two consecutive specimens establishes a diagnosis of active infection.

ULTRASOUND

The infection may be either acute or chronic. Ultrasound signs of renal infection may be absent altogether, and this is the commonest scenario as the infective episode has often been successfully treated with antibiotics by the time the ultrasound scan is performed. The infection may be confined to the bladder, that is *cystitis*, in which case low-level echoes and/or hyperechoic debris may be identified, or may have progressed to the kidneys. Scarring and/or cortical thinning may be present in cases of repeated infections.

Pyelonephritis

Acute pyelonephritis

Acute inflammation of the kidney rarely results in any ultrasound abnormality. Occasionally the kidney may be enlarged and hypoechoic, the contrast between the kidney and the hepatic or splenic parenchyma increasing due to oedema, but the ultrasound changes are generally subtle. The normally clear differentiation between the cortex and the medullary pyramids may become indistinct, but again may go unrecognized. CT is useful for detecting subtle inflammatory changes within the kidney.

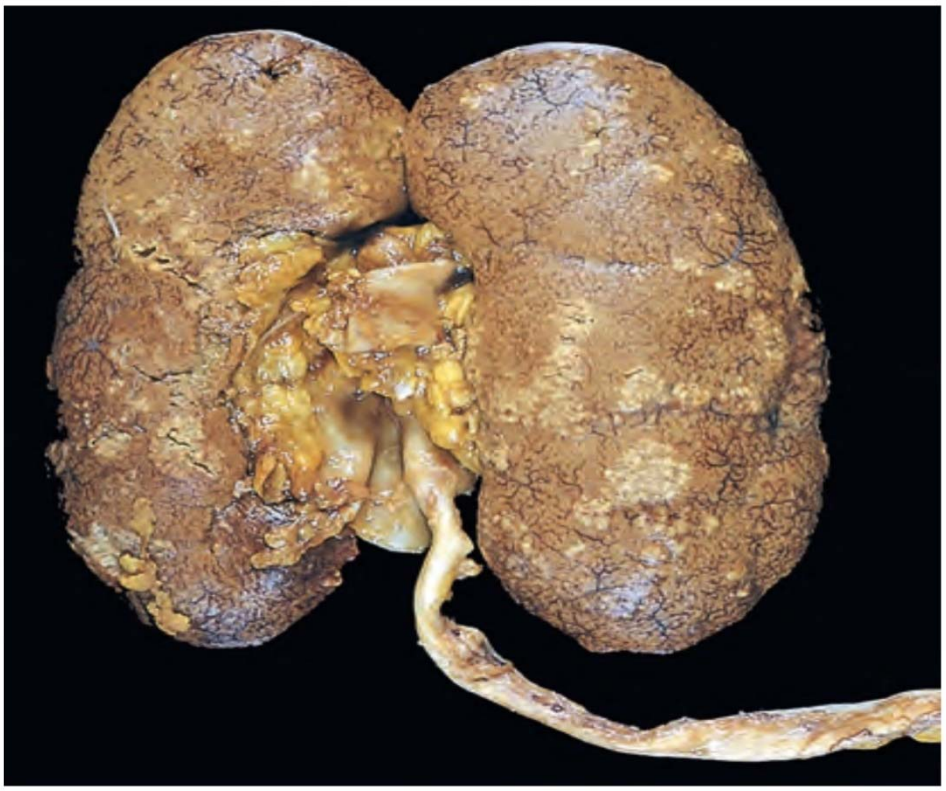


Figure 9.

Chronic pyelonephritis

This chronic inflammatory state is usually the result of frequent previous inflammatory/infective episodes. The kidney may be small and often has focal scarring present. Scar tissue has the appearance of a hyperechoic, linear lesion which affects the smooth renal outline and crosses the renal cortex . (Do not confuse focal scarring with fetal lobulation: the latter is smooth, thin, continuous with the capsule and forms an indentation between the pyramids.) The renal cortex is frequently thin in chronic pyelonephritis and may appear abnormally hyperechoic.

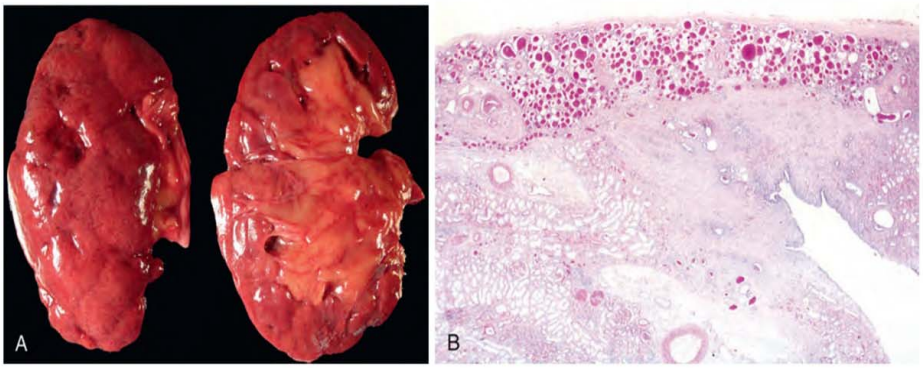


Figure 20-32 A, Chronic pyelonephritis. The surface *(left)* is irregularly scarred. The cut section *(right)* reveals blunting and loss of several papillae. **B,** Low-power view showing a corticomedullary renal scar with an underlying dilated deformed calyx. Note the thyroidization of tubules in the cortex.

Figure 10.

Bladder diverticula

Repeated infections can cause the bladder wall to thicken and become trabeculated. In such cases, a bladder diverticulum may form, making treatment of subsequent infections particularly difficult. The diverticulum may harbour debris or stones and may fail to empty properly, often enlarging as the urine refluxes into it when the patient micturates .

Focal pyelonephritis

The presence of acute infection within the kidney may progress in focal regions of the renal parenchyma. This phenomenon is particularly associated with diabetics. The ultrasonic changes are subtle, as in diffuse pyelonephritis, but it is possible to detect a slight change in echogenicity when it is surrounded by normal-looking parenchyma. Focal

pyelonephritis (sometimes called focal nephronia) may be either hypo- or hyperechoic compared with normal renal tissue. Depending on the size of the lesion, it may cause a mass effect, mimicking a renal tumour. The outline of the kidney is preserved, however the patient presents with fever and tenderness on the affected side and frequently has a history of urinary tract infection. A focal renal mass under these circumstances is highly suggestive of focal pyelonephritis and is also well demonstrated on CT[25]. It usually responds to antibiotic therapy and resolution of the lesion can be monitored with ultrasound scans. Focal pyelonephritis can progress to form an abscess in the kidney, which can normally be treated by percutaneous drainage and antibiotics.

Renal abscess

A renal abscess is generally a progression of focal inflammation within the kidney. The area liquefies and may enlarge to form a complex mass with distal acoustic enhancement. Low-level echoes from pus may fill the abscess cavity, giving it the appearance of increased echogenicity, but it may also be hypoechoic. The margins of the abscess may be ill-defined at first but may develop a more obvious capsule as the lesion becomes established , this capsule often has an easily identifiable thick rim. Flow may be seen in the inflammatory capsule with colour Doppler, but not in the liquefied centre. A renal abscess may mimic a lymphoma as

both may be hypoechoic on ultrasound, and both may have either single or multiple foci. The abscess may be intrarenal, subcapsular or perirenal. Frequently, drainage under ultrasound guidance is the preferred treatment; gradual resolution of the abscess can also be monitored with ultrasound.

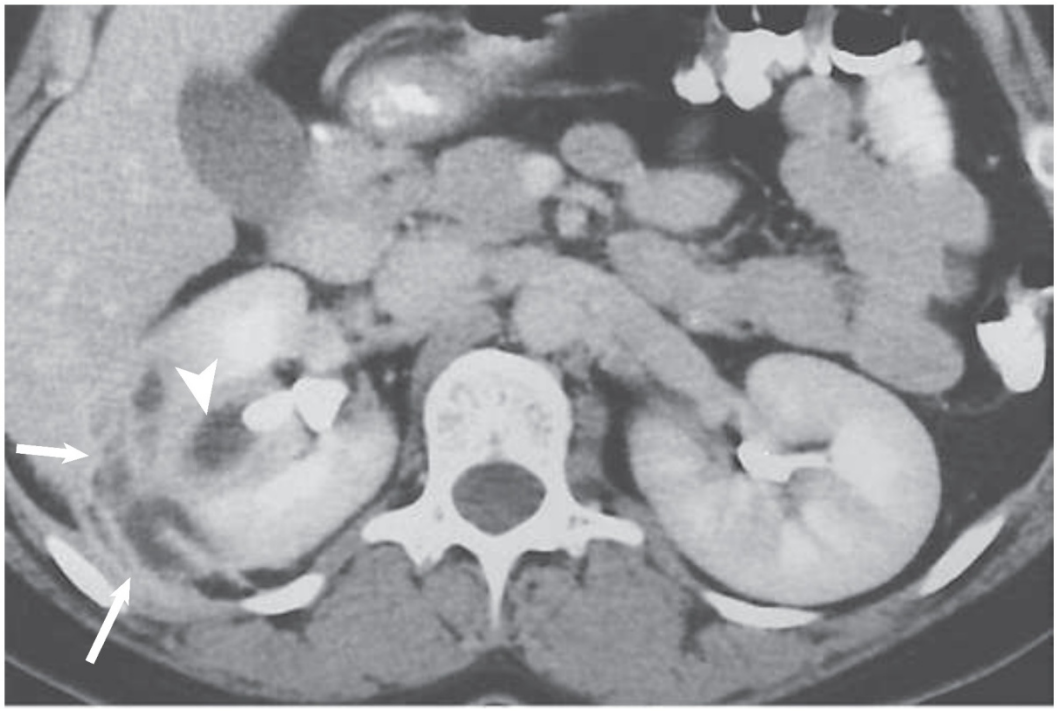


Fig. 51.6 Renal abscess. Contrast-enhanced CT scan shows an abscess in the medulla of the kidney *(arrowhead)* with penetration and extension into the perinephric space *(arrows)*. (Courtesy L. Towner.)

Picture 11:CT image of Renal abscess

Tuberculosis (TB)

Renal TB is an uncommon finding and a difficult diagnosis to make on ultrasound. The subtle inflammatory changes which affect the calyces in the early stages are best demonstrated with CT. In the later

stages ultrasound may show calcific foci and obstructed calyces as a result of thickened inflammatory calyceal walls, calcification and debris. TB frequently spreads to other adjacent sites in the abdomen, including the psoas muscle and gastrointestinal tract. The differential diagnosis is xanthogranulomatous pyelonephritis, which is often indistinguishable from TB on ultrasound, or a necrotic renal neoplasm.

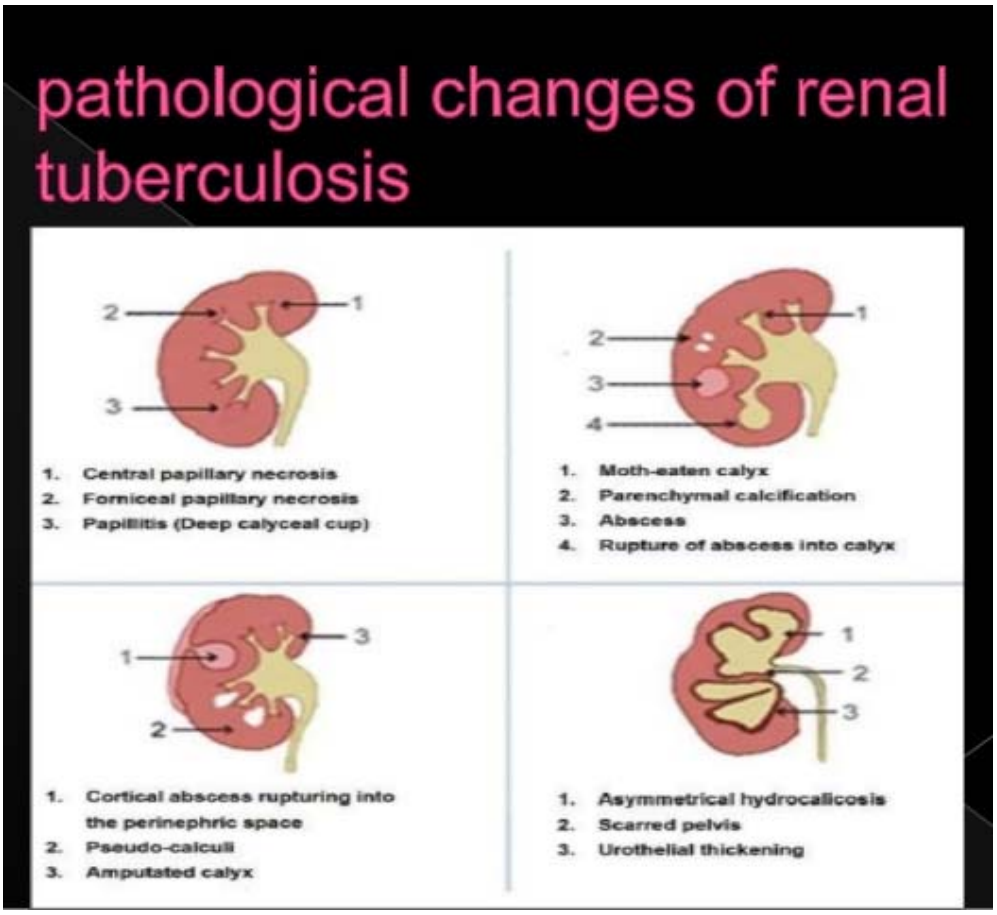


Figure 12.

Xanthogranulomatous pyelonephritis (XGP)

This condition (which gets its name from the yellow colour of the kidney) is the result of renal obstruction by calculi in the pelvicalyceal system. Frequently, a staghorn calculus is responsible. The kidney becomes chronically infected and the calyces enlarge and become filled with infected debris. The cortex may be eroded and thin. On ultrasound, these appearances are similar to TB or to a pyonephrosis. The latter is usually accompanied by a more severe, acute pain and fever whereas XGP or TB has a lower-grade, chronic pain. CT may differentiate TB from XGP and is also more sensitive to extrarenal spread of disease.

CT SCAN

Acute pyelonephritis

CT is the modality of choice for evaluating the parenchymal involvement of acute pyelonephritis, sometimes referred to as acute bacterial nephritis. It provides comprehensive anatomic and physiologic information that accurately characterizes both intrarenal and extrarenal pathologic conditions. Unenhanced CT is excellent for identifying urinary tract gas, calculi, hemorrhage, renal enlargement, inflammatory masses, and obstruction[26]. However, unenhanced CTimages may appear normal. On postcontrast studies, acute bacterial nephritis most commonly

manifests as one or more wedge-shaped areas or streaky zones of lesser enhancement that extend from the papilla to the renal cortex in the nephrographic phase, also known as striated nephrogram. In the delayed phase, reversal of the striated nephrogram occurs. Other findings include enlargement of the affected kidney due to edema, perinephric stranding, and areas of increased attenuation if hemorrhagic bacterial nephritis is present and thickening of the renal pelvis and ureteric wall. In progressive cases, a parenchymal abscess may develop. On CT, before liquefaction becomes evident, the abscess may resemble a renal mass, especially in the absence of typical clinical findings. Abscesses typically appear as round or geographic low-attenuation collections that do not enhance centrally but may have an enhancing rim . The rims are pseudocapsules with varied wall thicknesses and frequent nodularity. A halo of diminished enhancement may surround the abscess during the nephrographic phase. Extraparenchymal collections occasionally extend into adjacent structures, such as the psoas muscle. Persistent urinary leukocytes indicate residual inflammation that can usually be detected on CT[27,28].

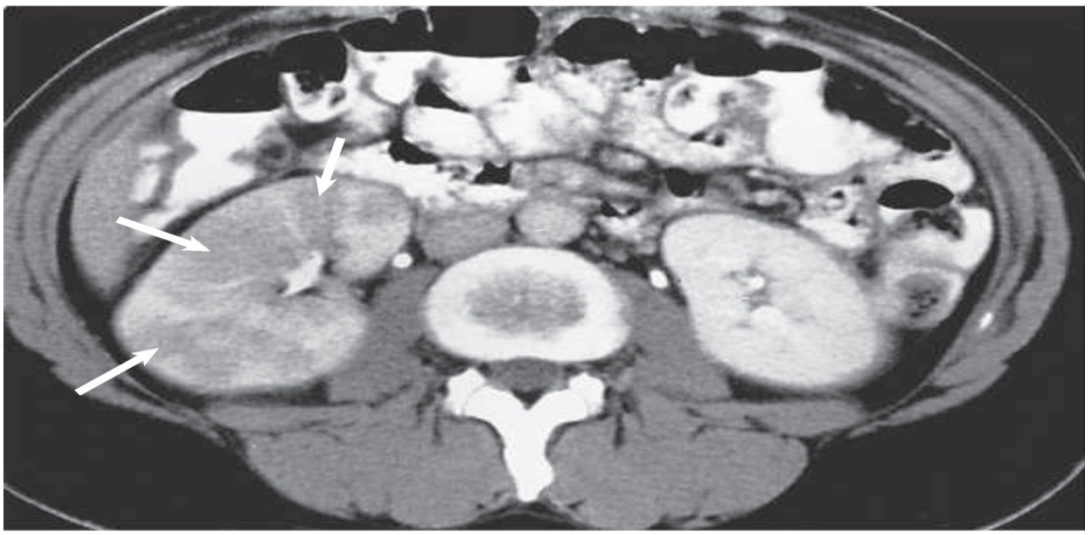


Fig. 51.4 Acute pyelonephritis. Contrast-enhanced CT scan shows areas of lower density caused by infection and edema *(arrows)*. (Courtesy W. Bush, University of Washington, Seattle, Wash.)

Picture 13:CT image of Acute Pyelonephritis

Chronic pyelonephritis

Imaging findings include renal scarring, atrophy, and cortical thinning; hypertrophy of residual normal tissue (which may mimic a mass lesion); calyceal clubbing secondary to retraction of the papilla from the overlying scar; dilatation of the calyceal system; and overall renal asymmetry.

Emphysematous Pyelonephritis

Two types of gas distribution have been reported. Type 1 (33 % of cases) is more aggressive and is characterized by renal parenchymal destruction that manifests with streaky or mottled areas of gas without intrarenal or extrarenal fluid collections . Type 2 (66 %) is less aggressive

andis characterized by renal or perirenal fluid collections associated with bubbly or loculated gas or by gas in the urinary collecting system.

Xanthogranulomatous Pyelonephritis

Diffuse (>80 %) or segmental imaging findings may be present. In the segmental form, the process may have the appearance of a renal mass and may be indistinguishable from RCC. In the more common diffuse form, the kidney is enlarged, with poor or no function. When extension occurs outside the kidney, it may involve the psoas muscle, and there may be fistulas to the abdominal wall. Most cases occur in association with a renal pelvic calculus; thus, hydronephrosis is thought to be a contributing factor[29]. CT is the imaging modality of choice for diagnosis and management. Findings include an enlarged kidney, with decreased or absent function; peripheral cystic dilatation; enhancing walls of the abscess cavities; perinephric extension; and a large central calculus. Stones are often laminated or branching in appearance.

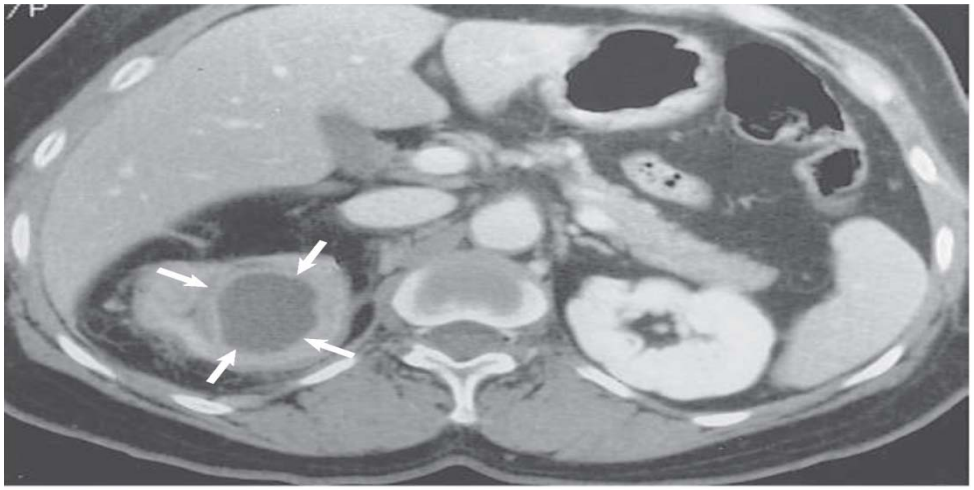


Fig. 51.9 Xanthogranulomatous pyelonephritis. Contrast-enhanced CT scan with the inflammatory mass outlined by *arrows*. Pathologic diagnosis confirmed xanthogranulomatous pyelonephritis. (Courtesy W. Bush, University of Washington, Seattle, Wash.)

Picture 15:CT image of XGPN

C Reactive Protein

CRP and many other APR can influence multiple stages of inflammation, and CRP has both pro inflammatory and anti inflammatory actions, although the primary effect may be anti inflammatory[30,31] . CRP can promote the recognition and elimination of pathogens and enhance the clearance of necrotic and apoptotic cells[32-38]. The protein consists of five identical, non-covalently associated subunits, each with a molecular weight of approximately 23 kD, which are arranged symmetrically around a central pore[39] . CRP and related proteins with this structure are termed pentraxins, which are a family of pattern recognition molecules involved in the innate immune response; others include serum amyloid P and a number of pattern recognition molecules referred to as long

pentraxins. A major function of CRP is its ability to bind phosphocholine, thereby permitting recognition both of foreign pathogens that display this moiety and phospholipid constituents of damaged cells . CRP can also activate the complement system and bind to phagocytic cells via Fc receptors, suggesting that it can initiate elimination of pathogens and targeted cells by interaction with both humoral and cellular effector systems of inflammation. These functions of CRP may have negative effects in some settings. As an example, CRP levels are increased in patients with immune thrombocytopenia (ITP), where CRP may amplify antibody-mediated platelet destruction upon binding to phosphocholine that is exposed after oxidation triggered by anti platelet antibodies. Pro inflammatory effects of CRP include activation of the complement system and the induction in monocytes of inflammatory cytokines and tissue factor and shedding of the IL-6 receptor . As a result, the CRP response to tissue injury may worsen tissue damage in some settings .

C-reactive protein — Elevations of CRP occur in association with acute and chronic inflammation due to a range of causes, including infectious diseases and non infectious inflammatory disorders. Very small changes in CRP levels, detected with highly-sensitive assays, may also occur in association with metabolic stresses in the absence of acute or chronic inflammatory states as they have traditionally been viewed.

'Normal' CRP levels

The level of CRP that is truly normal or clinically innocuous is not known. Data from a study conducted by the National Health and Nutrition Evaluation Survey of over 21,000 people in the United States revealed that CRP levels vary with age, sex, and race, with slightly higher levels seen with increased age, with female sex, and in African Americans . A rough correction of the CRP for age can be made by using the following formulas: the upper limit of the reference range (mg/dL) equals (age in years)/50 for men and (age in years/50) + 0.6 for women[40,41] . It is very important to note that there is no uniformity in the units that are used to report CRP levels. Some laboratories report CRP concentrations as mg/dL while others employ mg/L. Standard CRP determinations may be reported either in units of mg/dL or in units of mg/L, while determinations using a highly sensitive assay, generally referred to as "high-sensitivity CRP" (hs-CRP), are routinely reported in units of mg/L. Population studies reveal a skewed, rather than Gaussian, distribution of plasma CRP concentrations. About 70 to 90 percent of samples from reference populations have CRP concentrations under 0.3 mg/dL (3 mg/L), but some individuals have minor elevations up to 1 mg/dL (10 mg/L). What we commonly call normal ranges (properly called reference ranges) for CRP vary greatly from one laboratory to

another, to a degree that cannot be explained on a biologic or technical basis. What is thus regarded as "elevated" is often misleading. It would be best to regard CRP concentrations >1 mg/dL (10 mg/L) as indicating clinically significant inflammation while concentrations between 0.3 and 1 mg/dL (3 and 10 mg/L) indicate what is commonly referred to as low-grade inflammation. Low-grade inflammation is not accompanied by the classic signs of inflammation and may result from an immense number of metabolic stresses . Some of these stresses are clinically apparent; examples include atherosclerosis, obesity, obstructive sleep apnoea, insulin resistance, hypertension, and type 2 diabetes. Low grade inflammation is, however, also associated with an astounding number of conditions and lifestyles known to be associated with poor health, including low levels of physical activity, prehypertension , a large variety of unhealthy diets, social isolation, and even being unmarried .

Moderate to marked elevation of CRP — In most inflammatory conditions, the CRP, like the ESR, becomes elevated as part of the acute phase response. Markedly elevated levels of CRP are strongly associated with infection. Infections, most often bacterial, were found in approximately 80 percent of patients with values in excess of 10 mg/dL (100 mg/L) and in 88 to 94 percent of patients with values over 50 mg/dL (500 mg/L). Levels of CRP may also be elevated in patients with viral

infections, although usually not to the degree seen in patients with bacterial infection .ESR and CRP levels may be discrepant due to differences in kinetics, with the CRP both rising and decreasing more rapidly; or related to characteristics of the inflammatory or and immune-disease related mechanisms, as in systemic lupus, where significant CRP elevations are typically not as common or to as great a degree as are increases in the ESR.

High-sensitivity CRP and low-grade inflammation;

Some confusion has arisen because of widespread use of the terms "high-sensitivity CRP" and "low-grade inflammation" . One common misunderstanding has been the incorrect belief that hs-CRP is different in some way from the CRP that has been measured for many years. It is not. "High-sensitivity" only means that the concentration of CRP was determined using an assay designed to measure and distinguish very low levels of CRP. The CRP that is measured has no new or unique properties . Minor CRP elevation (concentrations between 3 and 10 mg/L) has been generally regarded as a marker of what has been called low-grade inflammation. However, this poorly defined state, sometimes referred to as mini inflammation or subclinical inflammation, occurs in many conditions in which there are minor degrees of metabolic dysfunction, such as obesity and insulin resistance, unlike inflammation as it has

traditionally been understood. Moreover, the low-grade inflammatory state differs in several important ways from the acute inflammation that occurs in response to infection or tissue injury[42,43]. The acute inflammatory state is associated with the classic signs of inflammation (swelling, erythema, warmth, and pain), while low-grade inflammation is not. Acute inflammation generally shows a marked CRP response while low-grade inflammation shows only minor CRP elevation. The inflammatory response to infection and tissue injury supports host defense, clearance of necrotic tissue, adaptation, and repair, while the purpose of low grade inflammation appears to be restoration of metabolic homeostasis. The factors that trigger the acute inflammatory response and low-grade inflammation differ as well. Acute inflammation is largely triggered by components of an invading pathogen, referred to as pathogen-associated molecular patterns (PAMPs), and by products of damaged cells, damage- (or danger-) associated molecular patterns (DAMPs). The latter are sometimes referred to as alarmins . One molecular mechanism that can trigger low-grade inflammation and CRP induction in response to metabolic stress that has been well-studied is the unfolded protein response . These differences between acute inflammation and low-grade inflammation are so great that two leading researchers in the field have suggested distinct nomenclatures for the latter; both "para-inflammation" and "metaflammation" (metabolically-

triggered inflammation) have been proposed to emphasize the distinction between metabolic perturbation and inflammation as it is traditionally viewed, both of which may result in increases in CRP levels.

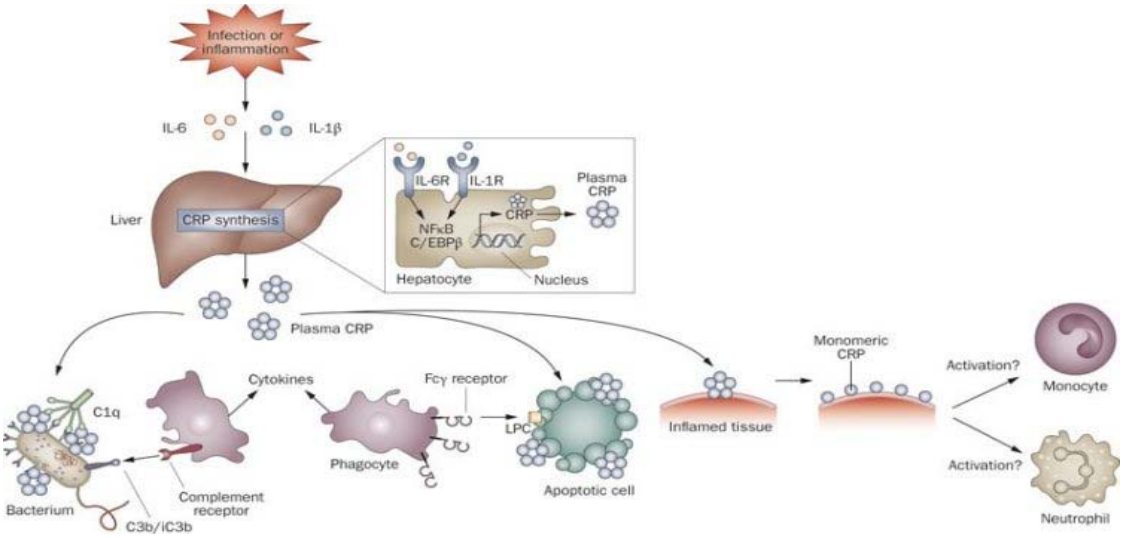


Figure 17.

TREATMENT OF UTI;

TABLE 51.6 Oral Regimens for Acute Uncomplicated Pyelonephritis and Complicated Urinary Tract Infection*,†

Drug	Dose (mg)	Interval	Comment
Fluoroquinolones			Preferred for empiric treatment; avoid if possible in pregnancy, nursing mothers, or persons younger than 18 years of age.
Ciprofloxacin	500	q12h	
Ciprofloxacin extended release	1000	q24h	
Levofloxacin	250-750	q24h	
Trimethoprim-sulfamethoxazole	160/800	q12h	Use only when the causative pathogen is known to be susceptible. If used in pregnancy (not approved use), avoid in first trimester.
Cefpodoxime proxetil	200	q12h	Data are sparse; use only when the causative pathogen is known to be susceptible.
Amoxicillin-clavulanate	500/125 to 875/125	q12h	Use only when the causative pathogen is known to be susceptible or in addition to a broad-spectrum agent when empiric coverage against enterococci is desirable.

*A long-acting parenteral antibiotic should be given concomitantly if there are concerns about drug resistance.
†Duration depends on clinical setting (see text and Fig. 51.5).

Picture 18:Oral medications for UTI

TABLE 51.5 Parenteral Regimens for Acute Uncomplicated Pyelonephritis and Complicated Urinary Tract Infection*

Drug	Dose (mg)	Interval
Ceftriaxone	1000-2000	q24h
Cefepime	1000-2000	q12h
Fluoroquinolones†		
Ciprofloxacin	200-400	q12h
Levofloxacin	250-750	q24h
Gentamicin† (± ampicillin)	3-5 mg/kg body weight	q24h
	1 mg/kg body weight	q8h
Ampicillin (+ gentamicin†)	1000	q6h
Trimethoprim-sulfamethoxazole†	160/800	q12h
Aztreonam	1000	q8-12h
Piperacillin-tazobactam	3375	q6-8h
Imipenem-cilastatin†,‡	250-500	q6-8h
Meropenem‡	500	q8h
Ertapenem‡	1000	q24h
Ceftolozane/tazobactam	1500	q8h
Ceftazidime/avibactam	2500	q8h
Vancomycin§	1000	q12h

*Duration depends on clinical setting (see text and Fig. 51.5).
†Avoid, if possible, in pregnancy.
‡Recommended if ESBL Enterobacteriacea is suspected or known. Ertapenem is not indicated for suspected or known *Pseudomonas* infection.
§Recommended if methicillin-resistant *Staphylococcus aureus* (MRSA) is suspected or known.

Picture 19:Parenteral Management of UTI

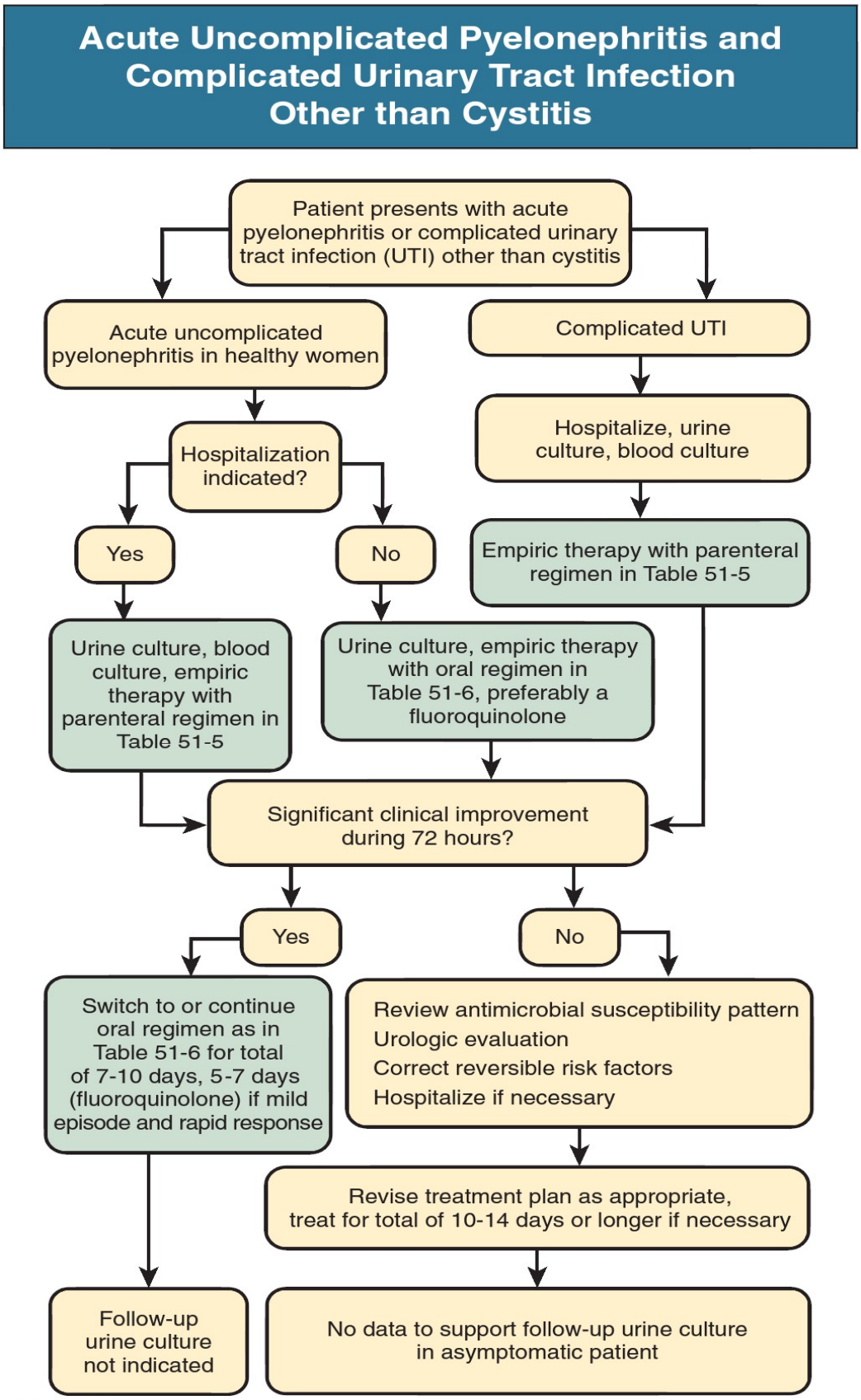


Fig. 51.5 Management algorithm for acute uncomplicated pyelonephritis and complicated urinary tract infection other than cystitis.

Picture 20

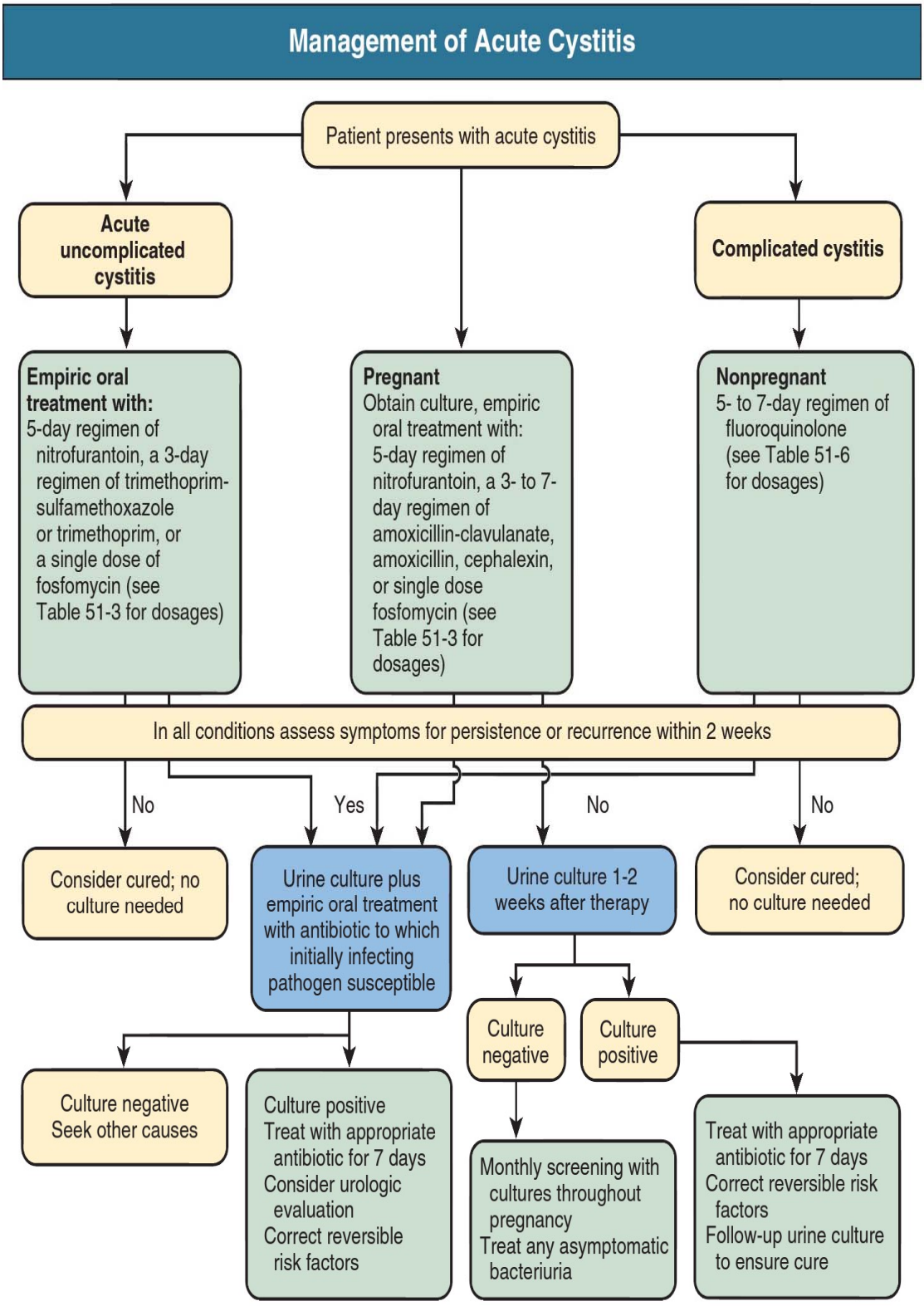


Fig. 51.1 Algorithm for management of acute cystitis.

Picture 21

TABLE 51.3 Oral Antimicrobial Agents for Acute Uncomplicated Cystitis

Drug	Dose (mg)	Interval*	Comment
Nitrofurantoin			Less active against *Proteus* spp.
Monohydrate/macrocrystals	100	q12h	
Macrocrystals	50	q6h	
Trimethoprim-sulfamethoxazole (TMP-SMX)	160/800	q12h	If used in pregnancy (not approved use), avoid in first trimester.
Trimethoprim	100	q12h	If used in pregnancy (not approved use), avoid in first trimester.
Fosfomycin	3000	Single dose	Less effective than fluoroquinolone or TMP-SMX.
Pivmecillinam	400	q12h	Availability limited to some European countries; not available for use in North America. Associated with minimal resistance and propensity for collateral damage, but efficacy rates are lower than other agents.
Cefpodoxime proxetil	100	q12h	Comparable to TMP-SMX, inferior to ciprofloxacin in 3-day regimen[35]
Amoxicillin-clavulanate	500/125	q12h	Inferior to ciprofloxacin in 3-day regimen[34]
Amoxicillin	500	q12h	Used only when causative pathogen is known to be susceptible or for empiric treatment of mild cystitis in pregnancy
Fluoroquinolones			
Ciprofloxacin	250	q12h	Avoid fluoroquinolones if possible in pregnancy, nursing mothers, or persons younger than 18 years old. Although highly effective, should be considered second-line treatment to preserve their usefulness for other infections. Moreover, in the United States, the FDA has stated that the risks of systemic fluoroquinolone antibacterial drugs outweigh their benefits for uncomplicated cystitis.
Ciprofloxacin extended release	500	q24h	
Levofloxacin	250	q24h	
Ofloxacin	200	q12h	

*Duration of therapy depends on the clinical setting (see text and Fig. 51.1); *q6h, q12h, q24h,* every 6, 12, or 24 hours.
FDA, U.S. Food and Drug Administration.

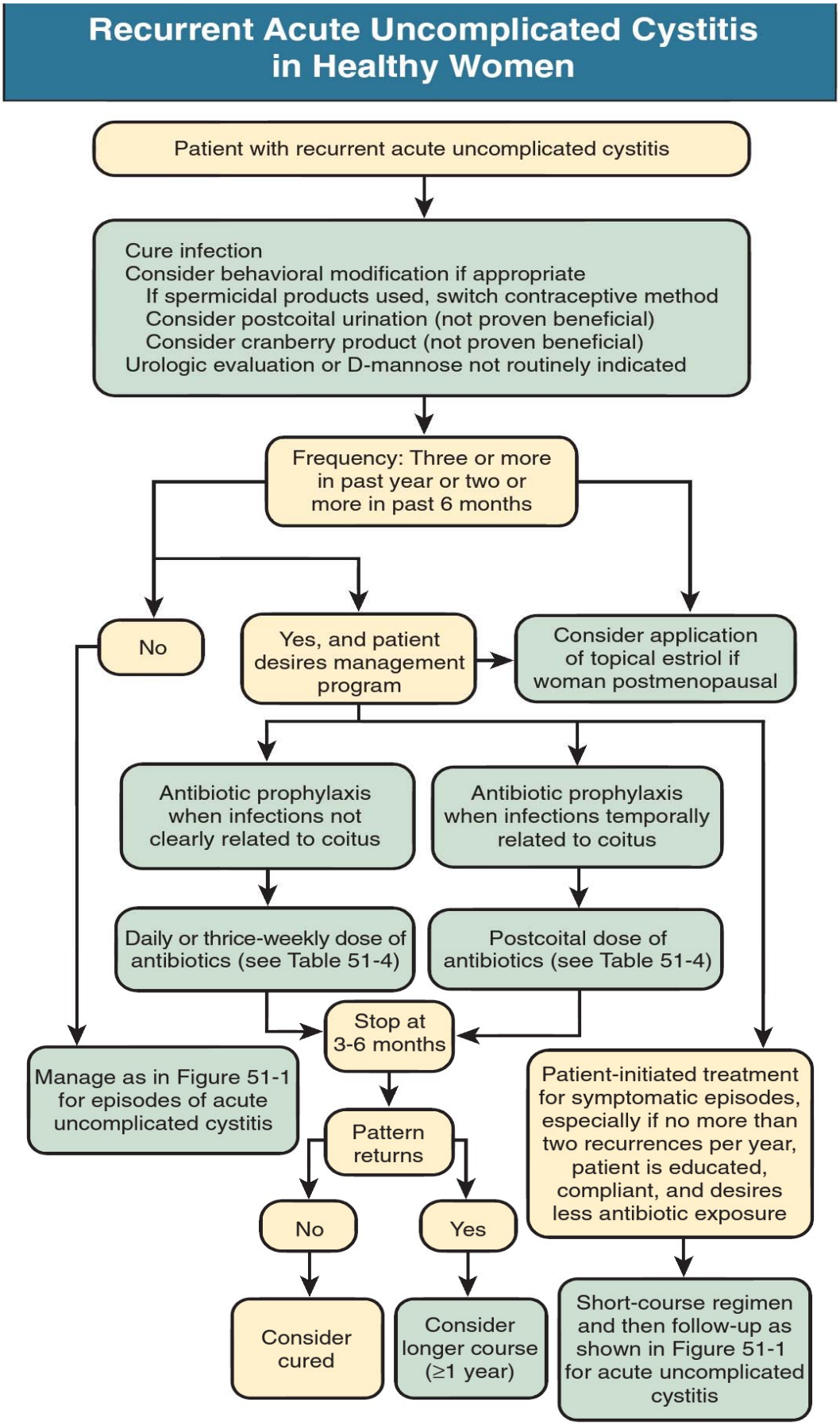
Picture 22

TABLE 51.4 Antimicrobial Prophylaxis Regimens for Women With Recurrent Acute Uncomplicated Cystitis*

Drug	Dose (mg)	Frequency
Continuous Prophylaxis		
Nitrofurantoin	50 or 100	Daily
TMP-SMX	40/200	Daily
TMP-SMX	40/200	Three times weekly
Trimethoprim	100	Daily
Cefaclor	250	Daily
Cefalexin (cephalexin)	125 or 250	Daily
Norfloxacin*	200	Other fluoroquinolones are likely to be as effective.†
Postcoital Prophylaxis		
Nitrofurantoin	50 or 100	Single dose
TMP-SMX	40/200	Single dose
TMP-SMX	80/400	Single dose
Cefalexin	250	Single dose
Ciprofloxacin*	125	Single dose
Norfloxacin*	200	Single dose
Ofloxacin*	100	Single dose

*See text and Fig. 51.2 for management strategy.
†Women should be cautioned about pregnancy when fluoroquinolones are being used. Fluoroquinolones are highly effective but not recommended, especially given the recent FDA warning that the risks of systemic fluoroquinolone antibacterial drugs outweigh their benefits for uncomplicated cystitis.

Picture 23


Recurrent Acute Uncomplicated Cystitis in Healthy Women
Patient with recurrent acute uncomplicated cystitis
Cure infection
Consider behavioral modification if appropriate
If spermicidal products used, switch contraceptive method
Consider postcoital urination (not proven beneficial)
Consider cranberry product (not proven beneficial)
Urologic evaluation or D-mannose not routinely indicated
Frequency: Three or more in past year or two or more in past 6 months
No
Yes, and patient desires management program
Consider application of topical estriol if woman postmenopausal
Antibiotic prophylaxis when infections not clearly related to coitus
Antibiotic prophylaxis when infections temporally related to coitus
Daily or thrice-weekly dose of antibiotics (see Table 51-4)
Postcoital dose of antibiotics (see Table 51-4)
Stop at 3-6 months
Manage as in Figure 51-1 for episodes of acute uncomplicated cystitis
Pattern returns
Patient-initiated treatment for symptomatic episodes, especially if no more than two recurrences per year, patient is educated, compliant, and desires less antibiotic exposure
No
Yes
Consider cured
Consider longer course (≥1 year)
Short-course regimen and then follow-up as shown in Figure 51-1 for acute uncomplicated cystitis

Picture 24

MATERIALS AND METHODS

Study center;

Institute of Internal Medicine Madras Medical College and Rajiv Gandhi Government General Hospital. Chennai-03.

Study Design;

Single center Observational Study

Sample size;

100 patients with urinary tract infection attending Internal Medicine OPD or admitted in wards based on inclusion & exclusion criteria. The required sample size was calculated based on the formula 4* (prevalence of disease)*

(1- prevalence of disease) / Error range.

Collaborating Departments;

Institute of Microbiology, MMC & RGGGH,CH-3.

Institute of Radiology ,MMC & RGGGH,CH-3.

Institute of Biochemistry ,MMC & RGGGH,CH-3.

Study Duration;

- 1 year

Study plan;

Based on previous studies, the mean value of C-reactive protein in upper urinary tract infection was 116.9 mg/L and lower urinary tract infection was 14.5 mg/L[44]. About 100 patients attending general medicine OPD and admitted in general medicine wards were subjected to detailed history taking, clinical examination and investigations such as CBC, Urine culture & Sensitivity, Serum CRP levels, USG KUB,CT-KUB(whenever necessary).

Inclusion criteria;

Patients with urine samples showing positive urine culture and patients showing symptoms of UTI.

Exclusion criteria;

Patients with inflammatory conditions other than UTI, history of trauma, pregnancy, USG proven renal calculi.

Serum CRP Assay Method:

C-reactive protein (CRP) levels in human serum based on the catalytic activity of gold nanoparticles and luminol-H_2O_2 chemiluminescence. The Chemiluminescence intensity in the presence of CRP and its ligand, O phosphorylethanolamine, was greatly enhanced due to the aggregation of Gold Nano Particles after the addition of 0.5M NaCl.

Statistical Analysis Plan:

Data analysed using statistical package - SPSS Software

Consent

All participants / attenders gave written informed consent.

Ethical Committee Approval

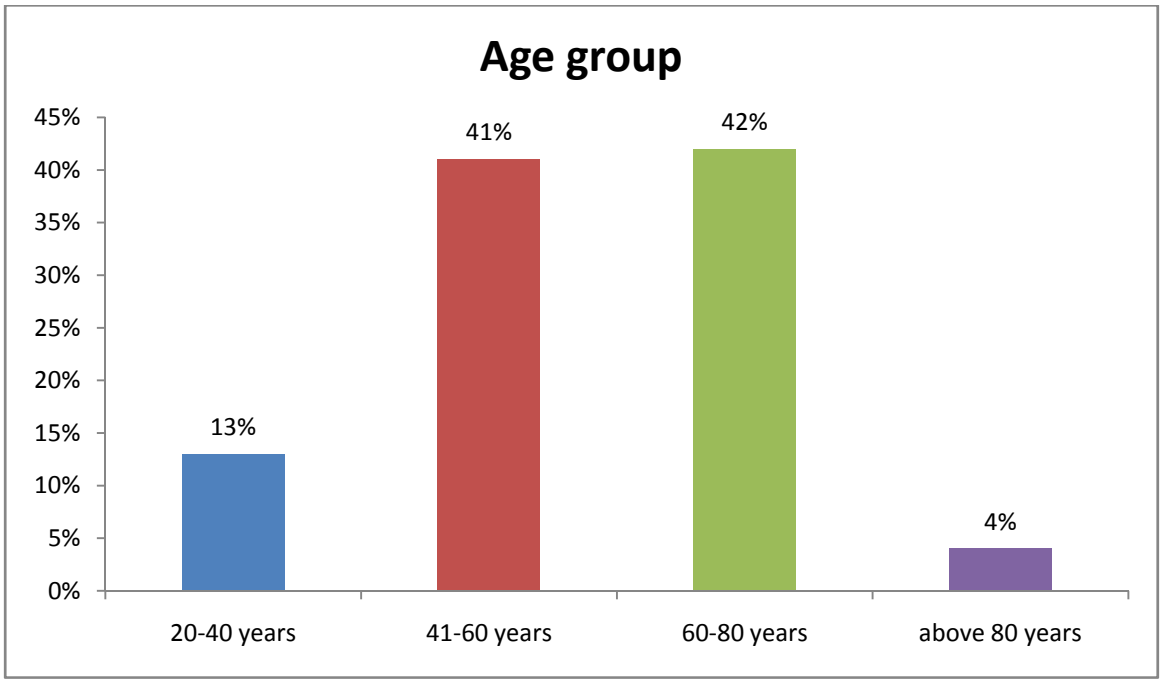
Institutional Ethics Committee of Madras Medical College approved the study.

RESULTS

Among 100 patients with UTI, 13% of patients belong to the age group of 20-40 years, 41% between 41-60 years, 42% between 61-80 years and 4% of them was above 80 years. The proportion of subjects in each group among various age range are given in table-1 and figure-25.

Age group	Frequency	Percent
20-40 years	13	13.0
41-60 years	41	41.0
61-80 years	42	42.0
above 80 years	4	4.0
Total	**100**	**100.0**

Table 1:Age distibution of patients with UTI



Picture 25:Age distribution of subjects

Among 100 cases ,26 were males and 74 were females.

Table 2: Sex wise distribution of cases

SEX	Frequency	Percent
Male	26	26.0
Female	74	74.0
Total	**100**	**100.0**

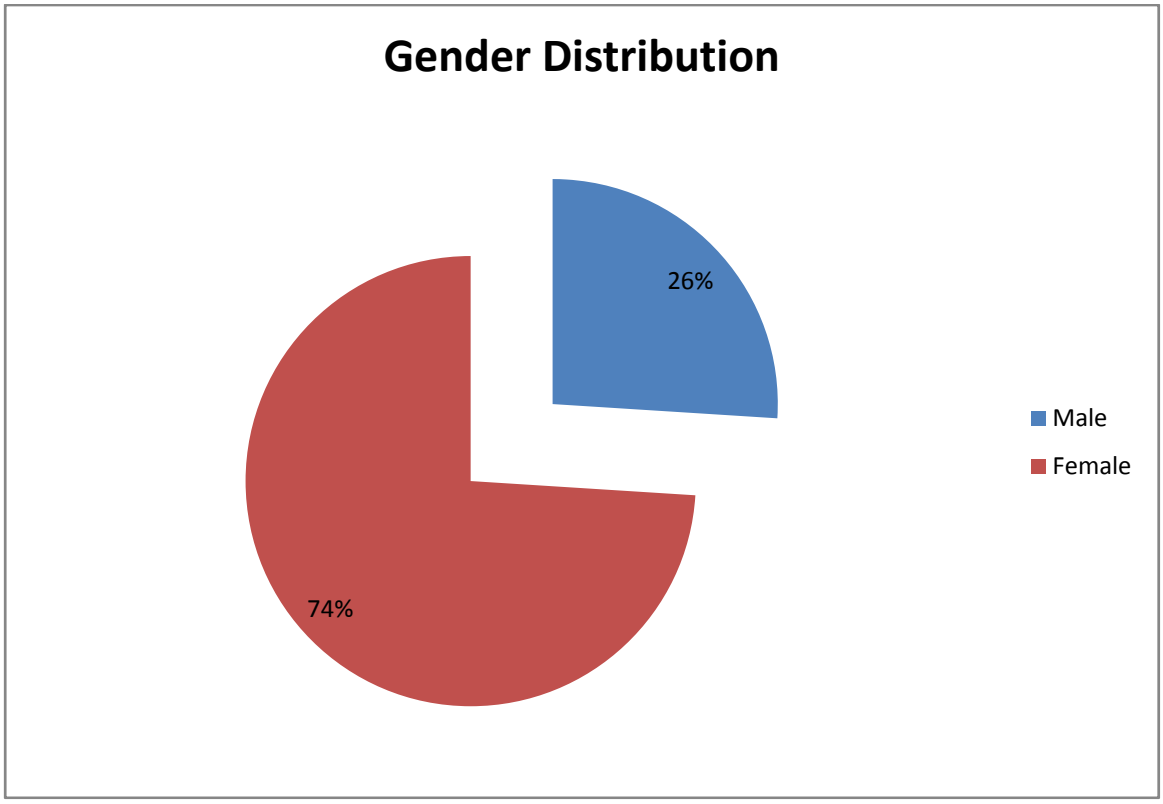


Figure 26:Gender Distribution of patients

The most common accompanying illness in patients include DM only comprising of about 38%,plus BPH and Cerebrovascular Accident each occupying 2%.

COMORBIDITIES	Frequency	Percent
BPH	4	4.0
CVA	4	4.0
DM	38	38.0
DM,BPH	2	2.0
DM,CVA	2	2.0
DM,SHT	1	1.0
Nil	49	49.0
Total	100	100.0

Table 3: Accompanying Illness in UTI

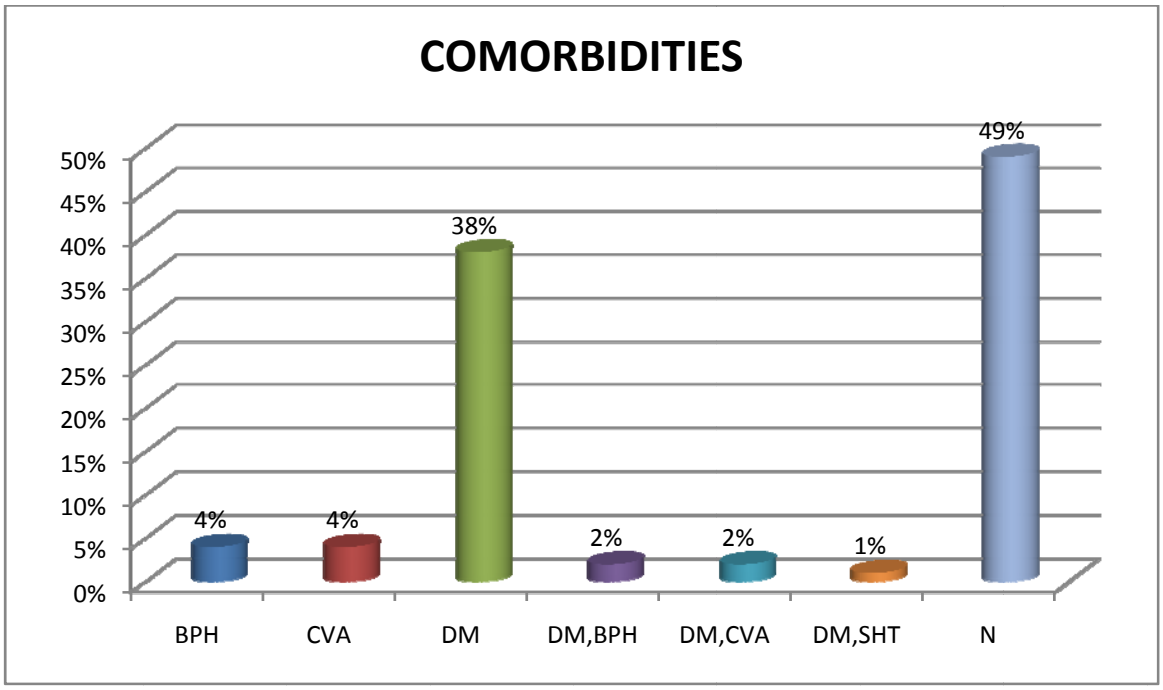


Figure 27.

Patients with a diagnosis of Lower urinary tract infection occupy 55% and upper UTI about 45%.

Location of UTI	Frequency	Percent
lower	55	55.0
Upper	45	45.0
Total	100	100.0

Table 4.

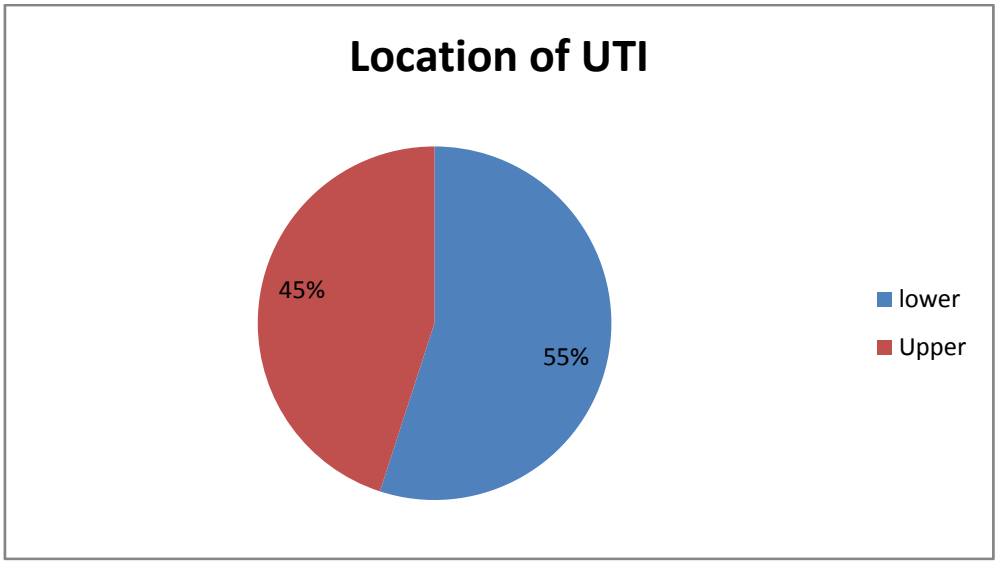


Figure 28.

The most common symptoms in patient with lower urinary tract infection include Dysuria(85%), lower abdominal pain(25%), urgency(16%), frequency(13%).

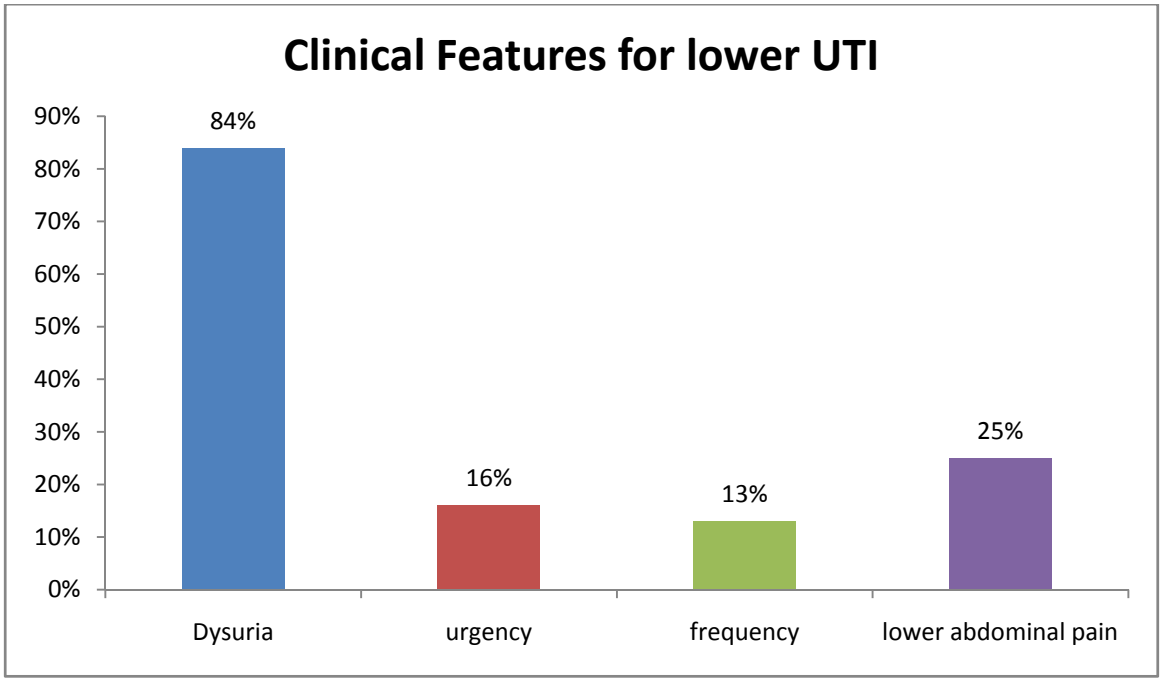


Figure 29.

		%
Dysuria	46	84%
urgency	9	16%
frequency	7	13%
lower abdominal pain	14	25%

Table 4.

The symptoms in patients with infection involving upper urinary tract include Fever (96%),chills(38%),vomiting (36%),loin pain(18%), Diabetic ketoacidosis (13%).

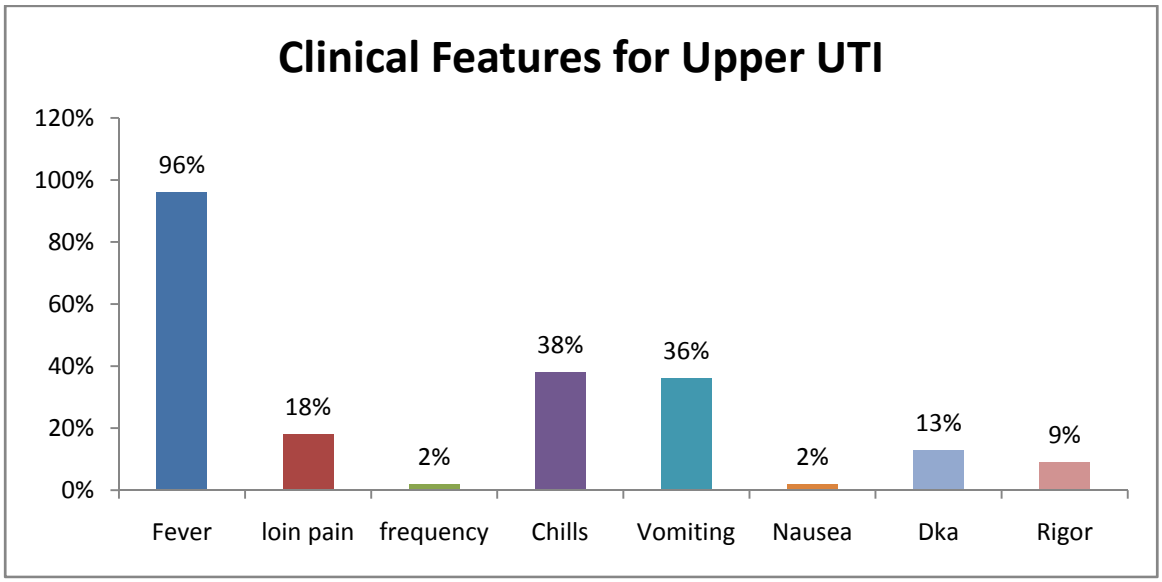


Figure 30

Fever	43	96%
Loin pain	8	18%
Urgency,Frequency	1	2%
Chills	17	38%
Vomiting	16	36%
Nausea	1	2%
DKA	6	13%
Rigor	4	9%

Table 5.

The bacterial organisms in UTI was of gram negative bacilli of which E.coli was most common present in about 73%.

URINE CULTURE	Frequency	Percent
Acinetobacter	1	1.0
E.coli	73	73.0
klebsiella	4	4.0
Normal	16	16.0
Proteus	2	2.0
Pseudomonas	4	4.0
Total	**100**	**100.0**

Table 6.

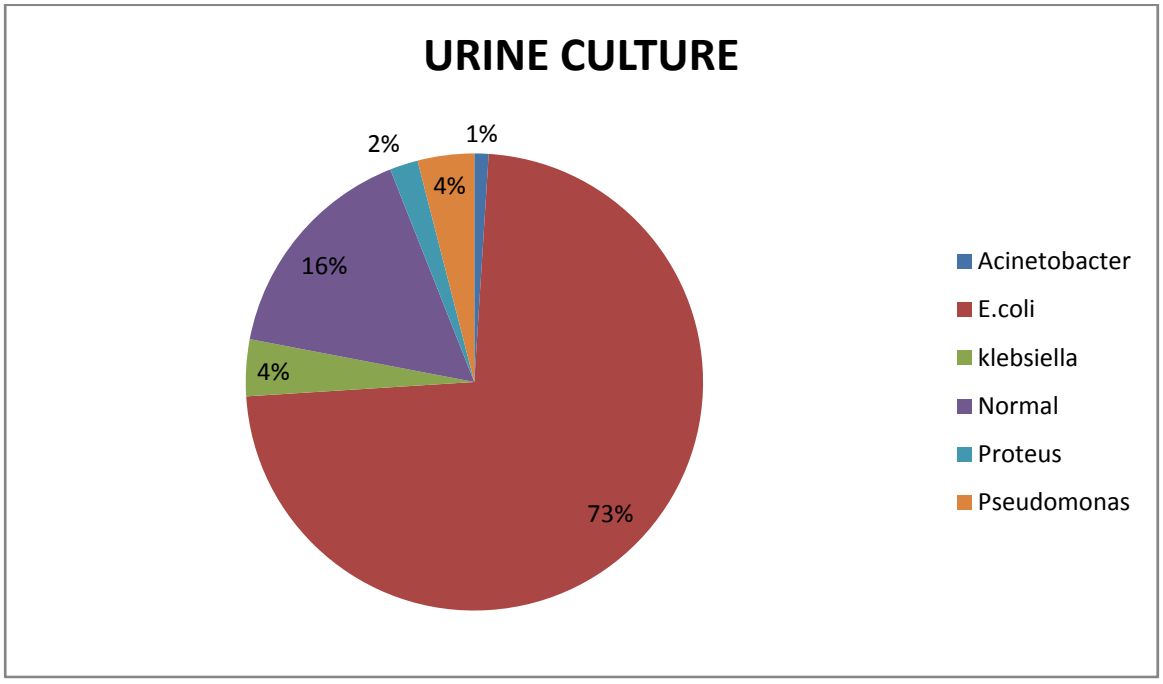


Figure 31.

Ultrasound abdomen & pelvis was done in all patients with symptoms of urinary tract infection which showed cystitis in 30 out of 55 patients with lower urinary tract infection.Other significant findings include prostatomegaly, pyelonephritis, Hydroureteronephrosis.

USG KUB	Frequency	Percent
Grade 1 prostatomegaly	5	5.0
Grade 2 prostatomegaly	2	2.0
Lt.pyelonephritis	2	2.0
Normal	43	43.0
Cystitis	30	30
Rt.HUN	6	6.0
Rt.pyelonephritis	12	12.0
Total	**100**	**100.0**

Table 7.

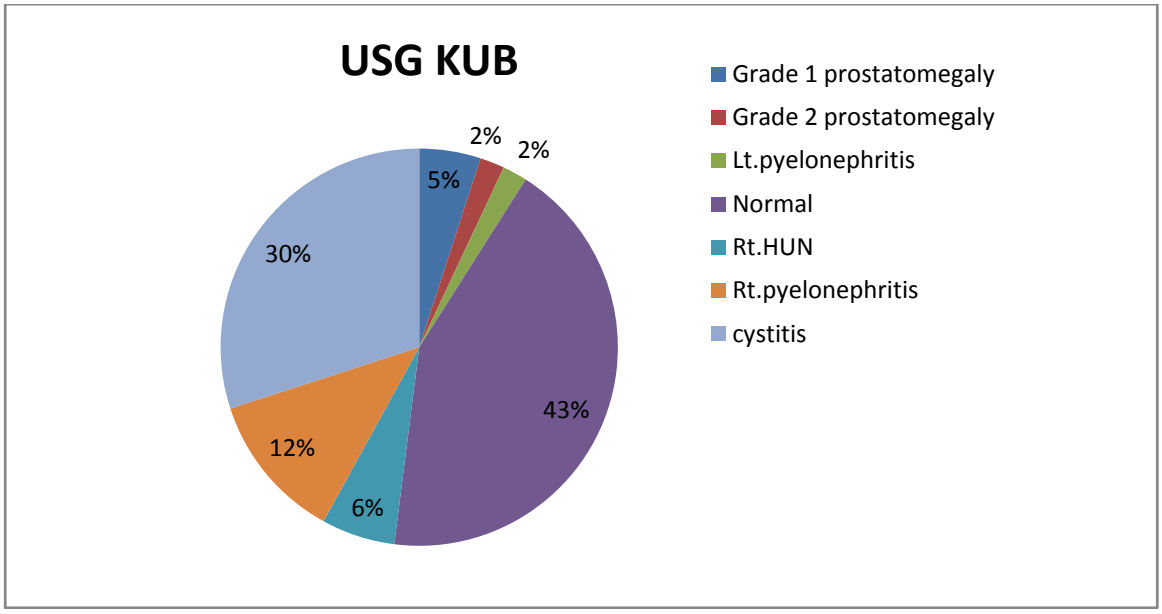


Figure 32.

Non contrast CT-KUB was done in all patients with symptoms of upper urinary tract infection which showed better diagnostic value compared to ultrasound abdomen.

CT KUB(IF DONE)	Frequency	Percent
B/L Pyelonephritis	4	8.5%
Lt.pyelonephritis	15	31.9%
Lt.pyelonephritis with HUN	1	2.1%
Normal	2	4.3%
Rt.HUN	1	2.1%
Rt.pyelonephritis	18	38.3%
Rt.pyelonephritis with HUN	6	12.8%
Total	**47**	**100.0%**

Table 8.

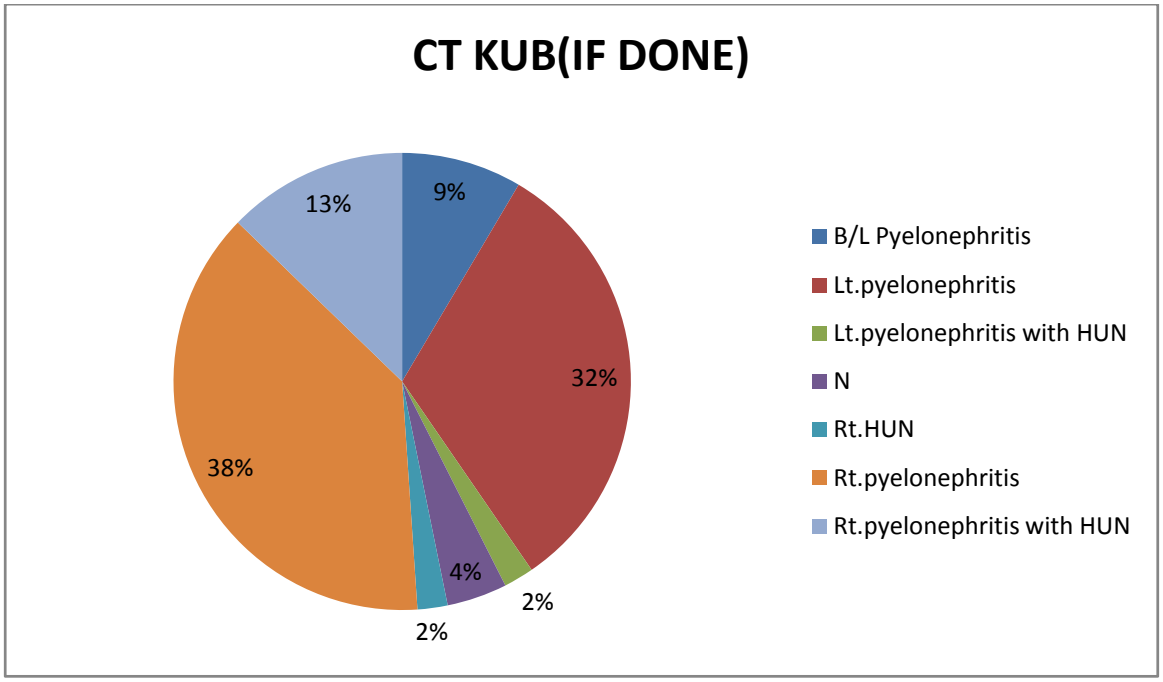


Figure 33.

The mean value of CRP in subjects with upper UTI(159.20) was significantly higher than the mean value of lower UTI(16.16).

Group Statistics

	Location of UTI	N	Mean	Std. Deviation	Std. Error Mean	Z test
CRP LEVELmgL	lower	55	16.1564	10.40704	1.40329	8.574**
	Upper	45	159.2089	49.12149	7.32260	

**p<0.001

Table 9.

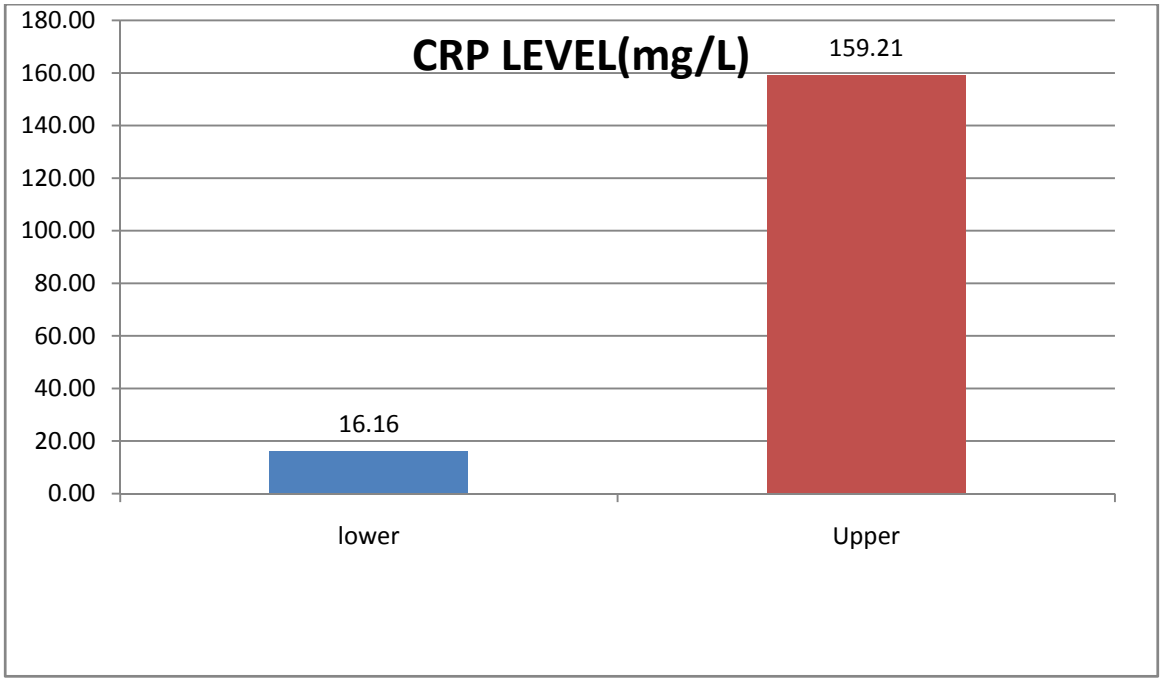


Figure 34.

			Statistic
CRP LEVELmgL	Mean		80.5300
	95% Confidence Interval for Mean	Lower Bound	64.8465
		Upper Bound	96.2135
	Median		31.9000
	Variance		6247.492
	Std. Deviation		79.04108
	Minimum		1.50
	Maximum		249.50

Table 10.

	Location of UTI			Statistic
CRP LEVELmgL	lower	Mean		16.1564
		95% Confidence Interval for Mean	Lower Bound	13.3429
			Upper Bound	18.9698
		5% Trimmed Mean		16.0212
		Median		14.2000
		Variance		108.307
		Std. Deviation		10.40704
		Minimum		1.50
		Maximum		33.50
	Upper	Mean		155.8756
		95% Confidence Interval for Mean	Lower Bound	139.5811
			Upper Bound	172.1701
		5% Trimmed Mean		157.0210
		Median		166.8000
		Variance		2941.618
		Std. Deviation		54.23668
		Minimum		5.00
		Maximum		249.50

.

Table 11

			CRP level 123		Total
			<31.9 Median	>31.9 Median	
age group	20-40 years	Count	6	7	13
		%	12.0%	14.0%	13.0%
	41-60 years	Count	20	21	41
		%	40.0%	42.0%	41.0%
	60-80 years	Count	20	22	42
		%	40.0%	44.0%	42.0%
	above 80 years	Count	4	0	4
		%	8.0%	0.0%	4.0%
Total		Count	50	50	100
		%	100.0%	100.0%	100.0%

Pearson Chi-Square=4.197 p=0.241

Table 12.

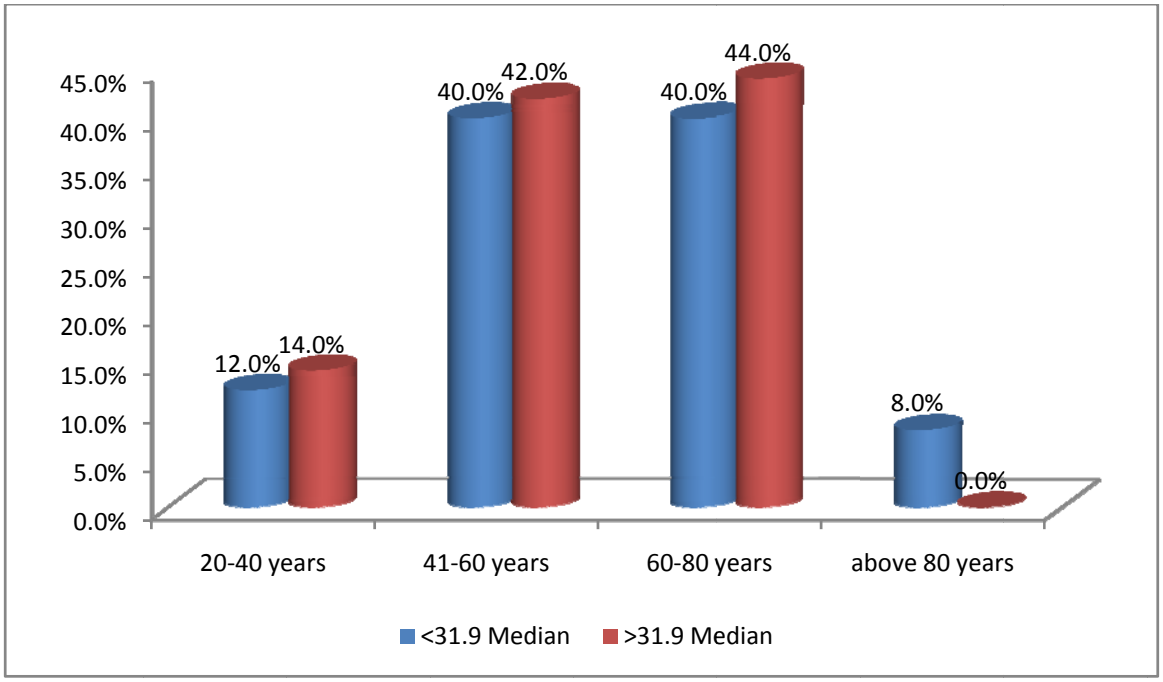


Figure 35.

			CRP level 123		Total
			<31.9 Median	>31.9 Median	
SEX	Male	Count	9	17	26
		%	18.0%	34.0%	26.0%
	Female	Count	41	33	74
		%	82.0%	66.0%	74.0%
Total		Count	50	50	100
		%	100.0%	100.0%	100.0%

Pearson Chi-Square=3.326 p=0.068

Table 13.

			CRP level 123		Total
			<31.9 Median	>31.9 Median	
Comorbidities	BPH	Count	2	2	4
		%	4.0%	4.0%	4.0%
	CVA	Count	3	1	4
		%	6.0%	2.0%	4.0%
	DM	Count	10	28	38
		%	20.0%	56.0%	38.0%
	DM,BPH	Count	0	2	2
		%	0.0%	4.0%	2.0%
	DM,CVA	Count	0	2	2
		%	0.0%	4.0%	2.0%
	DM,SHT	Count	1	0	1
		%	2.0%	0.0%	1.0%
	N	Count	34	15	49
		%	68.0%	30.0%	49.0%
Total		Count	50	50	100
		%	100.0%	100.0%	100.0%

Pearson Chi-Square=21.894** p<0.001

Table 14.

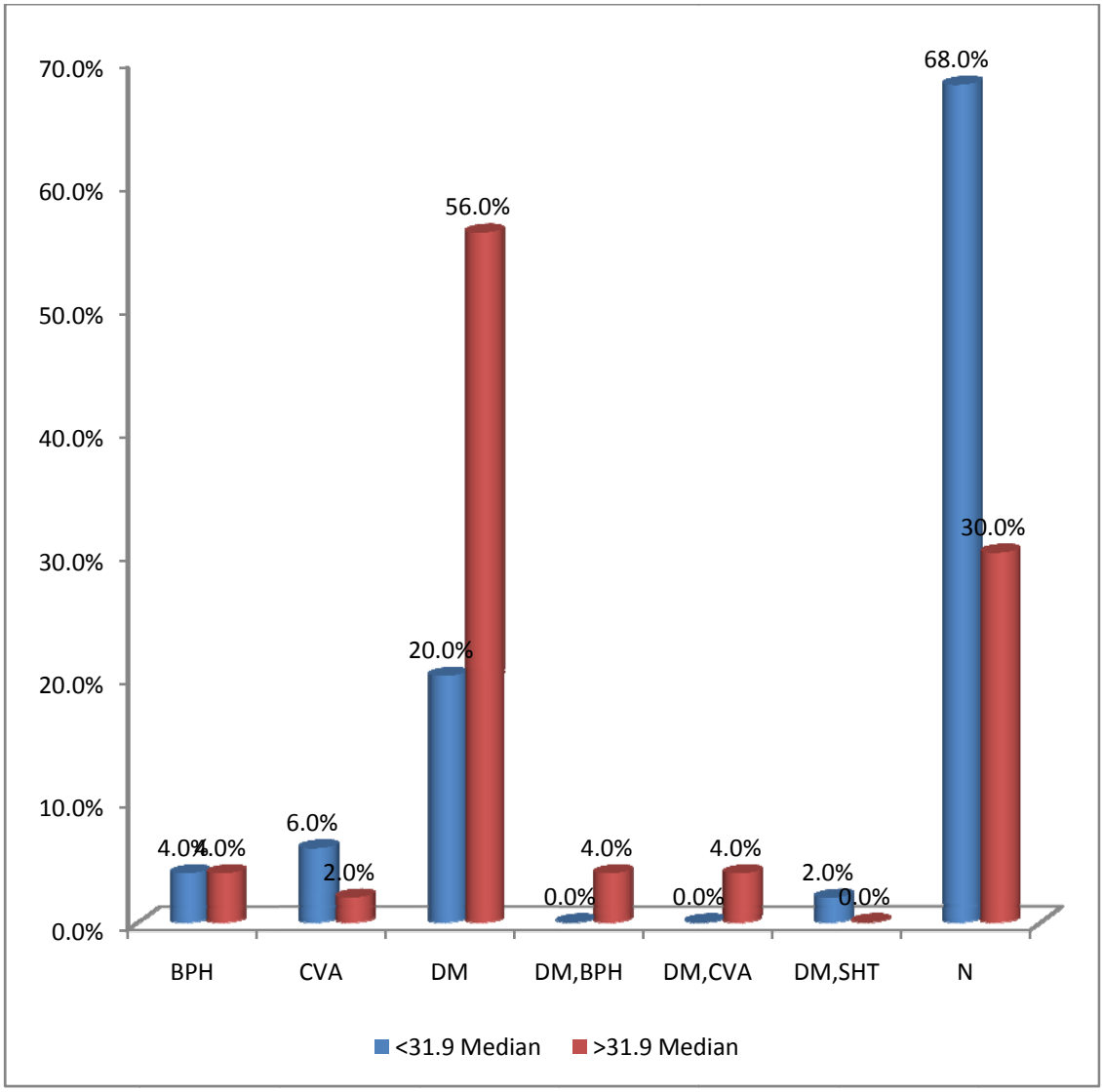
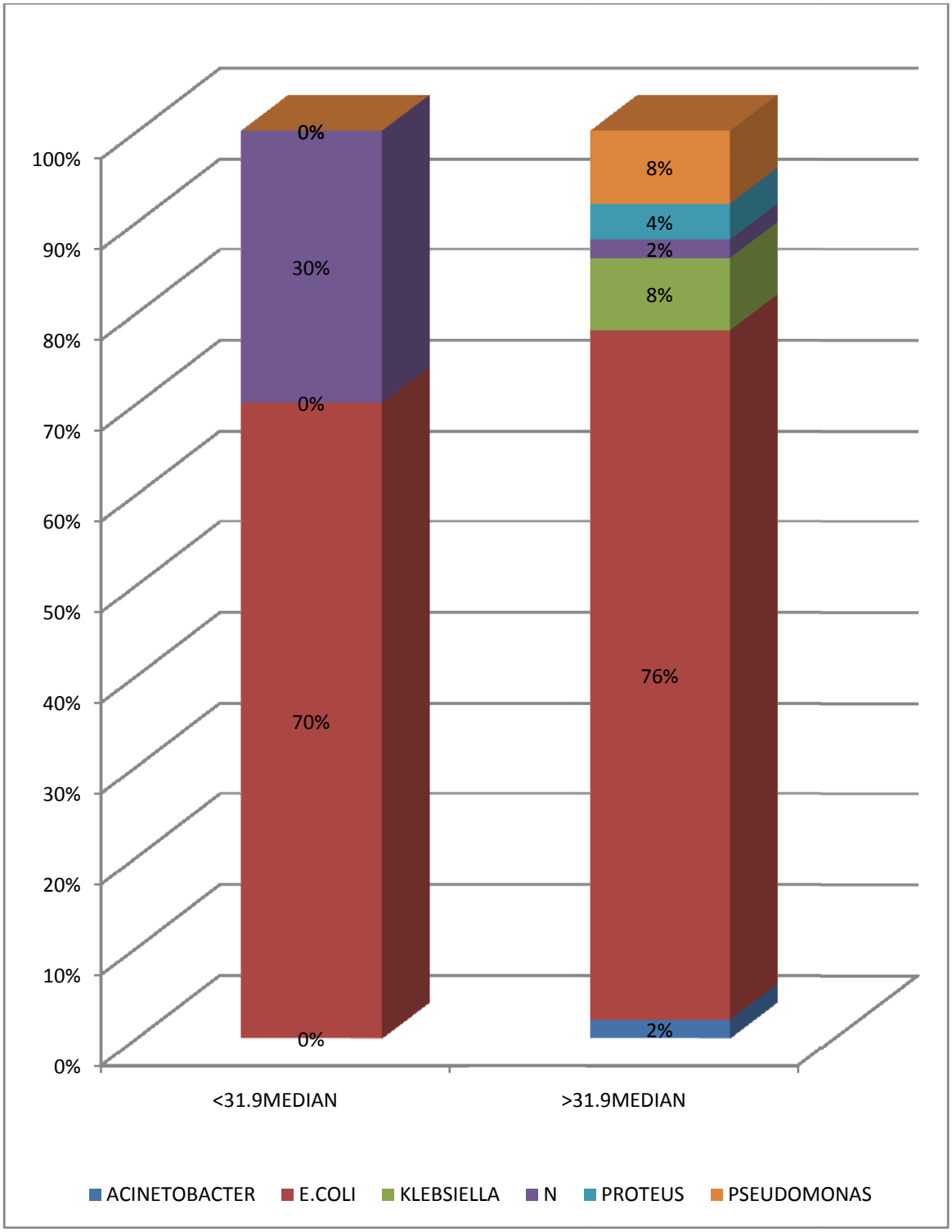

70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
4.0%
4.0%
6.0%
2.0%
20.0%
56.0%
0.0%
4.0%
0.0%
4.0%
2.0%
0.0%
68.0%
30.0%
BPH
CVA
DM
DM,BPH
DM,CVA
DM,SHT
N
<31.9 Median
>31.9 Median

Figure 36.

			CRP level 123		Total
			<31.9 Median	>31.9 Median	
URINE CULTURE	Acinetobacter	Count	0	1	1
		%	0.0%	2.0%	1.0%
	E.coli	Count	35	38	73
		%	70.0%	76.0%	73.0%
	klebsiella	Count	0	4	4
		%	0.0%	8.0%	4.0%
	N	Count	15	1	16
		%	30.0%	2.0%	16.0%
	Proteus	Count	0	2	2
		%	0.0%	4.0%	2.0%
	Pseudomonas	Count	0	4	4
		%	0.0%	8.0%	4.0%
Total		Count	50	50	100
		%	100.0%	100.0%	100.0%

Pearson Chi-Square=23.373 ** p<.001

Table 15.


100%
90%
80%
70%
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50%
40%
30%
20%
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0%
0%
30%
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70%
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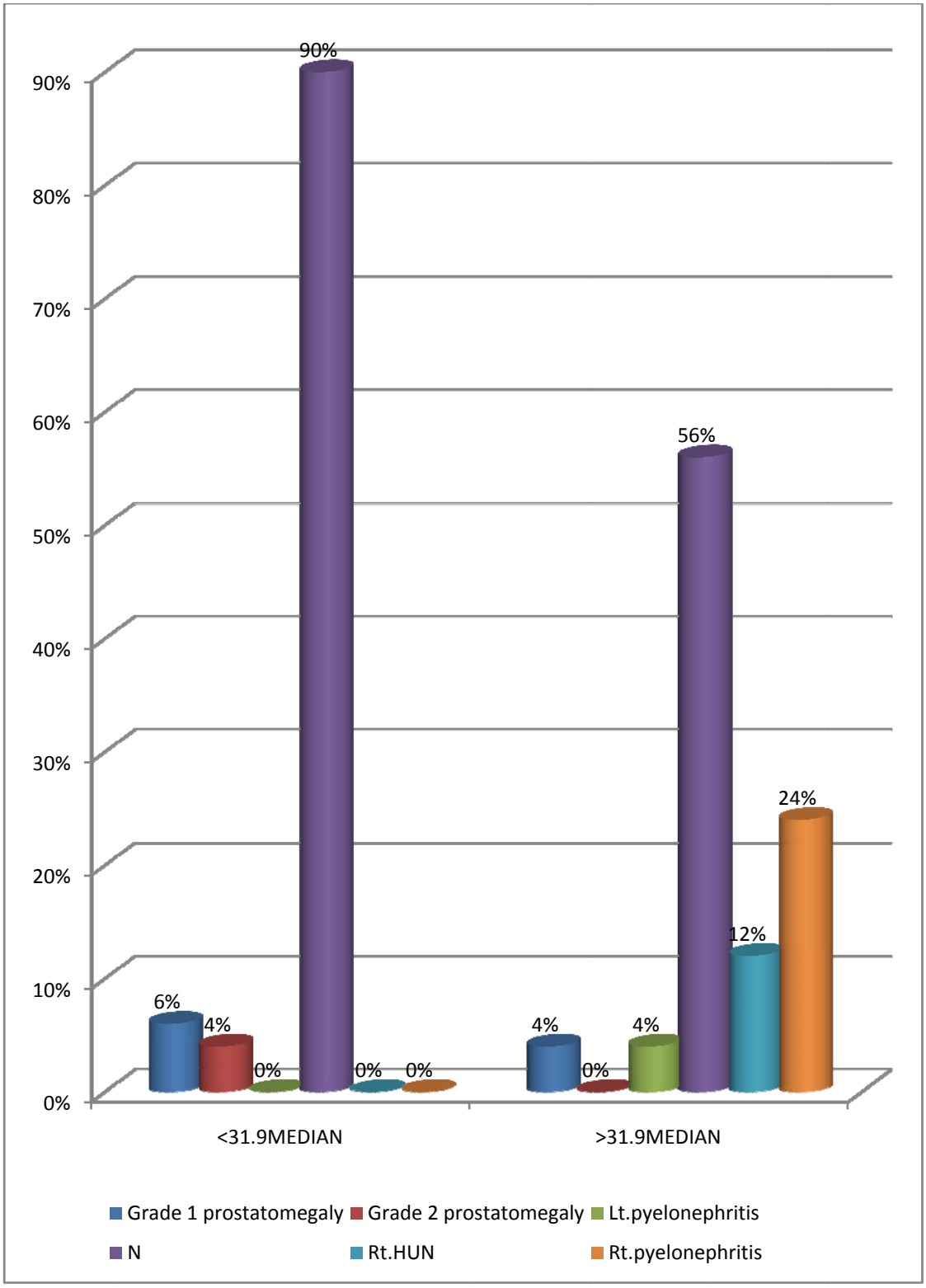
8%
4%
2%
8%
76%
2%
<31.9MEDIAN
>31.9MEDIAN
ACINETOBACTER
E.COLI
KLEBSIELLA
N
PROTEUS
PSEUDOMONAS

Figure 37.

			CRP level 123		Total
			<31.9 Median	>31.9 Median	
USG KUB	Grade 1 prostatomegaly	Count	3	2	5
		%	6.0%	4.0%	5.0%
	Grade 2 prostatomegaly	Count	2	0	2
		%	4.0%	0.0%	2.0%
	Lt.pyelonephritis	Count	0	2	2
		%	0.0%	4.0%	2.0%
	Normal study	Count	45	28	73
		%	90.0%	56.0%	73.0%
	Rt.HUN	Count	0	6	6
		%	0.0%	12.0%	6.0%
	Rt.pyelonephritis	Count	0	12	12
		%	0.0%	24.0%	12.0%
Total		Count	50	50	100
		%	100.0%	100.0%	100.0%

Pearson Chi-Square=26.159 ** p<.001

Table 16.


90%
80%
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60%
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30%
20%
10%
0%
6%
4%
0%
90%
0%
0%
4%
0%
4%
56%
12%
24%
<31.9MEDIAN
>31.9MEDIAN
Grade 1 prostatomegaly
Grade 2 prostatomegaly
Lt.pyelonephritis
N
Rt.HUN
Rt.pyelonephritis

Figure 38.

			CRP level 123		Total
			<31.9 Median	>31.9 Median	
CT KUB(IF DONE)		Count	48	5	53
		%	96.0%	10.0%	53.0%
	B/L Pyelonephritis	Count	0	4	4
		%	0.0%	8.0%	4.0%
	Lt.pyelonephritis	Count	0	15	15
		%	0.0%	30.0%	15.0%
	Lt.pyelonephritis with HUN	Count	0	1	1
		%	0.0%	2.0%	1.0%
	Normal	Count	2	0	2
		%	4.0%	0.0%	2.0%
	Rt.HUN	Count	0	1	1
		%	0.0%	2.0%	1.0%
	Rt.pyelonephritis	Count	0	18	18
		%	0.0%	36.0%	18.0%
	Rt.pyelonephritis with HUN	Count	0	6	6
		%	0.0%	12.0%	6.0%
Total		Count	50	50	100
		%	100.0%	100.0%	100.0%

Pearson Chi-Square=26.159** p<.0014

Table 17.

DISCUSSION

In UTI differentiation between upper and lower urinary tract infection has prognostic significance. The distinction between lower and upper tract infection is more important because renal involvement can induce parenchymal scarring that may lead to arterial hypertension and chronic renal failure.

The present study was undertaken to determine the levels of CRP in patients with the diagnosis of urinary tract infection and to compare the levels of CRP in relationship to upper and lower UTI. In the present study UTI was commonly seen in the age group between 40-80 years(83%) and predominantly involved female patients(74%).UTI was less commonly seen in young patients. In the age group of 20-40 years, only 13% had UTI. A similar result was observed by ML Pursnani et al. in which 65.52% cases were females and rest 34.48% cases were males.

Diabetes mellitus which have been considered as an important risk factor for UTI were evaluated in the present study. Majority of patients in this study have DM accounting for 38%% and 49% of cases presents with no comorbidities. In India, large number of populations is found be diabetics accounting for 32 million at present and is expected to rise to 57.2 million by 2025. Neutrophil chemotaxis and adherence to vascular endothelium, phagocytosis, intracellular

bactericidal activity, opsonization, and cell-mediated immunity are all depressed in diabetics with hyperglycemia predisposing them to increased susceptibility to infections. Other comorbid illness associated with urinary tract infection include prostatitic enlargement, cerebrovascular accident.

The results in present study showed that mean CRP level was found to be higher among patients with upper urinary tract infection (159.21mg/L) compared to lower urinary tract infection(16.16 mg/L).

Bharath MS et al. have studied the levels of CRP levels in patients with urinary tract infection and in their study the mean value of C-reactive protein in upper urinary tract infection was 116.9 mg/L and lower urinary tract infection was 14.5 mg/L . This shows that C-reactive protein is significantly raised in upper urinary tract infection. means that C-reactive protein can be used to diagnose inflammation in upper urinary tract infection. This confirms the observation of Gervaix, Alain MD et al, Stanley Haller stein et al (1982), Jodal and Hanson (1976), who studied the usefulness of sequential determination of C-reactive protein value in acute pyelonephritis. A study of Chieh-Wei Yen et al showed that longer febrile period and high C-reactive protein level are good indicators of prediction of the risk of pyelonephritis in urinary tract infection patients. Fever or an elevated C-reactive protein level often accompanies acute

pyelonephritis and is found in rare cases of cystitis but also occurs in infections other than pyelonephritis. Till date only a few studies are available in adult age group.

Xu et al. have found that the serum CRP levels of the Acute Pyelonephritis group were significantly higher than those of the lower UTI group (68.17 ± 39.42 mg/l vs. 21.39 ± 14.92 mg/l, $P < 0.01$,). Correlation analysis demonstrated that CRP were in a significantly positive correlation with a correlation coefficient of 0.729 ($P < 0.01$).

The organisms which were isolated in patients with urinary tract infection include E.coli(73%), klebsiella(4%) ,pseudomonas(4%), proteus(2%), acinetobacter(1%) and culture was normal in 16% of the patients who was previously treated with antibiotics. Moreover longer follow up studies with persistence of same degree of elevation of C-reactive protein may point to high risk cases which are likely to develop chronic parenchymal renal disease with hypertension in future.

CONCLUSION

- In the present study, serum CRP levels were found to be significantly higher in patients with upper urinary tract infection compared to lower urinary tract infection.
- Serum C-Reactive Protein level measurements can be done in patients with symptoms of urinary tract infection especially in individuals with risk factors such as Diabetes Mellitus to make an prediction of upper urinary tract involvement.
- Early initiation of empirical antibiotic therapy can be done as for Complicated UTI in patients with higher CRP levels to prevent renal scarring.
- CRP levels can also be used for observing pathogenesis and curative effect ,which is a non-invasive test and is not associated with morbidity and also economically feasible in tertiary and peripheral setting.

LIMITATIONS

- Sample size of the study is very small, hence further studies large number of cases is required.
- The study was conducted in patients admitted at a single tertiary care center.
- This was a cross sectional case control study and follow up details were not evaluated.
- Majority of the patients with UTI were females occupying nearly 75%.
- It was also very difficult to exclude other inflammatory conditions that can cause rise in C-Reactive Protein levels.

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A STUDY OF ROLE OR BLOOD CRP LEVELS IN UPPER AND LOWER URINARY TRACT INFECTIONS

Name :

Age/Sex :

OP/IP No :

Occupation :

Address :

Contact No. :

SYMPTOMS

- ◊ Fever
- ◊ Loin pain
- ◊ Dysuria
- ◊ Frequency
- ◊ Urgency

PATIENT CHARACTERISTICS

- ◊ Age
- ◊ sex
- ◊ pregnancy status

EXAMINATION

- ◊ Temperature
- ◊ Loin tenderness

URINE CULTURE &SENSITIVITY

CRP LEVEL;

INFORMATION SHEET

We are conducting a study on **"A STUDY TO DIFFERENTIATE UPPER AND LOWER TRACT INFECTIONS WITH BLOOD CRP LEVELS"** among patients attending Rajiv Gandhi Government General Hospital, Chennai and for that your specimen may be valuable to us.

The purpose of this study is to explore a diagnostic method to differentiate for upper and lower urinary tract infection .We are selecting certain cases and if you are found eligible, we may perform extra tests and special studies which in any way do not affect your final report or management.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator Signature of Participant

Date :

Place :

PATIENT CONSENT FORM

Study Detail	:	**A STUDY TO DIFFERENTIATE UPPER AND LOWER URINARY TRACT INFECTIONS WITH BLOOD CRP LEVELS**
Study Centre	:	Rajiv Gandhi Government General Hospital, Chennai.
Patient's Name	:	
Patient's Age	:	
Identification Number	:	

Patient may check (☑) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction.	
I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.	
I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the	

regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.	
I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms.	
I hereby consent to participate in this study.	
I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests.	

Signature/thumb impression Signature of Investigator

Patient's Name and Address **Dr.R.KRISHNA**

ஆய்வு ஒப்புதல் படிவம்

ஆய்வு தலைப்பு :

குருதி CRP அளவின் மூலம் மேல் சிறுநீர்க் குழாய் மற்றும் சிறுநீர்ப் பாதை தொற்று பிரித்தறிதலுக்கான ஓர் ஆய்வு

பெயர் :
வயது :
பால் :

தேதி :
வெளிநோயாளி எண் :
ஆராய்ச்சி சேர்க்கை எண் :

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது. எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்துகொண்டு நான் எனது சம்மதத்தை தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியில் குருதி CRP அளவின் மூலம் மேல் சிறுநீர்க் குழாய் மற்றும் சிறுநீர்ப் பாதை தொற்று பிரித்து ஆராயப்படுகிறது என்பதை ஆராய்ச்சியாளர் கூற அறிந்துகொண்டேன்.

மேற்கண்ட பரிசோதனையின் போது ஏற்படக்கூடிய பின்விளைவுகளையும் முழுவதும் உணர்ந்து இந்த பரிசோதனைக்கு மனமார சம்மதிக்கிறேன்.

நான் ஆராய்ச்சியாளருடன் ஒத்துழைப்பேன் என்றும், எனக்கு ஏற்படக்கூடிய ஆசாதாரண நிகழ்வுகள் பற்றியும் உடனடியாக ஆராய்ச்சியாளரிடம் தெரிவிப்பேன் என்று உறுதி கூறுகிறேன். இந்த ஆய்விலிருந்து எப்போது வேண்டுமானாலும் எக்காரணமும் கூறாமல் என்னை விடுவித்துக்கொள்ளலாம் என்பதை அறிவேன்.

என்னிடம் இருந்து பெறப்படும் தகவல்களை அரசு, வரைமுறை அதிகாரிகள் ஆகியோர்களுடன் பகிர்ந்துகொள்ள ஆராய்ச்சியாளருக்கு அனுமதி அளிக்கிறேன். என்னுடைய சிகிச்சைக்கட்டுகளை பார்வையிட உரிமை உண்டு. என்னுடைய தகவல்களின் அடையாளம் இரகசியமாக வைக்கப்படும் என்பதை அறிவேன்.

இந்த ஆராய்ச்சியில் பங்கேற்க தன்னிச்சையாக முழு மனதுடன் சம்மதிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம் / ரேகை

பங்கேற்பவர் பெயர்

இடம் :

தேதி :

ஆய்வாளர் கையொப்பம்

ஆய்வாளர் பெயர்

இடம் :

தேதி :

ETHICAL COMMITTEE APPROVAL FORM

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To

Dr.R.Krishna
I Year PG in MD General Medicine
Institute of Internal Medicine
Madras Medical College
Chennai 600 003

Dear Dr.R.Krishna,

The Institutional Ethics Committee has considered your request and approved your study titled "**A STUDY OF DIFFERENTIATE UPPER AND LOWER URINARY TRACT INFECTIONS WITH BLOOD CRP LEVELS "** - **NO.17062017(A)**

The following members of Ethics Committee were present in the meeting hold on **20.06.2017** conducted at Madras Medical College, Chennai 3

1. Prof.Dr.C.Rajendran, MD., :Chairperson
2. Prof.R.Narayana Babu,MD.,DCH., MMC,Ch-3 : Deputy Chairperson
3. Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3 :Member Secretary
4. Prof.S.Mayilvahanan,MD,Director,Inst. of Int.Med,MMC, Ch-3 : Member
5. Prof.A.Pandiya Raj,Director, Inst. of Gen.Surgery,MMC : Member
6. Prof.Rema Chandramohan,Prof.of Paediatrics,ICH,Chennai : Member
7. Prof. Susila, Director, Inst. of Pharmacology,MMC,Ch-3 : Member
8. Thiru S.Govindasamy, BA.,BL,High Court,Chennai : Lawyer
9. Tmt.Arnold Saulina, MA.,MSW., :Social Scientist
10. Tmt.J.Rajalakshmi, JAO,MMC, Ch-3 : Lay Person

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary - Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

PLAGIARISM REPORT

URKUND

Urkund Analysis Result

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Instances where selected sources appear:

9

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **"A STUDY TO DIFFERENTIATE UPPER AND LOWER URINARY TRACT INFECTIONS WITH BLOOD CRP LEVELS"** of the candidate **Dr**.**R.KRISHNA** with registration Number **201611011** for the award of **M.D.** in the branch of **GENERAL MEDICINE**. I personally verified the urkund.com website for plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **2 percentage** of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.